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INTRASPINAL LIPOMAS

REPORT OF CASES; REVIEW OF THE LITERATURE, AND CLINICAL AND PATHOLOGIC STUDY

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Masses of adipose tissue within the cranium and within the spinal canal not associated with bifid spines are rare. Intracranial lipoma, reported cases of which numbered 74 up to 1936 (Sperling and Alpers [1]), rarely produces clinical symptoms because of its small size, and no reported tumor of this sort had been attacked surgically. Intraspinal lipoma is even less common, but it frequently grows to enormous size, produces compression of the spinal cord and is surgically exposed. When it is encountered, its true nature is unsuspected until the yellow mass is visualized or, when the tumor is reddish or white, until histologic examination is made. Elsberg's [2] series of data on 267 cases of extramedullary tumors, compiled in 1941, included 6 instances of lipoma. It is probable, however, that the 2 tumors lying both intradurally and extradurally were associated with spina bifida, since Wolf,[3] in discussing what appears to be the same series of tumors, omitted them and noted that 1 of the 3 intradural tumors was associated with spina bifida. With the omission of these 2 tumors, lipomas constitute 1.5 per cent, or less, of extramedullary tumors. Steinke [4] reported data on 330 cases of tumors of the spinal cord collected from various sources. Among these cases were 4 instances of lipoma and 2 of angiolipoma (1.8 per cent). Von Lennep [5] tabulated data on 153 cases of tumors of the spinal cord from one clinic and included 2 cases of lipoma. Among 740 verified cases of tumors of the spinal cord data on which are in the files of the Mayo Clinic up to December 1942, there are 6 instances of lipoma (0.8 per cent). An additional tumor recently discovered brings the percentage to about 0.9. The over-all incidence appears to be close to 1 per cent of all primary intraspinal neoplasms.

The problem of which tumors to exclude as being merely masses of fat misplaced because of spina bifida has been handled differently by different authors. Spiller [6] included 3 cases which others, including us, would exclude because of an isthmus linking the intraspinal lesion with an extraspinal lipoma through a variety of bony defects. Other investigators (Wolbach and Millet [7]; Sachs and Fincher [8]) would discard the case of myolipoma reported by Gowers [9] because it is assumed that any tumor-bearing muscle must have come from the outside, despite the fact that no spina bifida

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1. Sperling, S. J., and Alpers, B. J.: Lipoma and Osteolipoma of the Brain, J. Nerv. & Ment. Dis. **83**: 13-21 (Jan.) 1936.

2. Elsberg, C. A.: Some Pathological Features of Primary and Secondary Extramedullary Tumors of the Spinal Cord, J. Mt. Sinai Hosp. **7**:247-258 (Jan.-Feb.) 1941.

3. Wolf, A.: Tumors of the Spinal Cord, Nerve Roots and Membranes: II. Pathology, in Elsberg, C. A.: Surgical Diseases of the Spinal Cord, Membranes, and Nerve Roots: Symptoms, Diagnosis, and Treatment, New York, Paul B. Hoeber, Inc., 1941, p. 349.

4. Steinke, C. R.: Spinal Tumors: Statistics on a Series of 330 Collected Cases, J. Nerv. & Ment. Dis. **47**:418-426 (June) 1918.

5. von Lennep, H.: Ueber Rückenmarkstumoren, Deutsche Ztschr. f. Chir. **160**:137-140 (Nov.) 1920.

6. Spiller, W. G.: Lipoma of the Filum Terminale, J. Nerv. & Ment. Dis. **26**:287-296, 1899.

7. Wolbach, S. B., and Millet, J. A. P.: Diffuse Sub-Dural Lipomatosis of the Spinal Cord in an Infant, Boston M. & S. J. **168**:681-682 (May) 1913.

8. Sachs, E., and Fincher, E. F.: Intramedullary Lipoma of the Spinal Cord: Complete Operative Removal, Arch. Surg. **17**:829-833 (Nov.) 1928.

9. Gowers, W. R.: Myo-Lipoma of the Spinal Cord, Tr. Path. Soc. London **27**:19-22, 1876.

	Year	Author	Sex	Age at Onset of Symptoms	Duration	Level	Position on Cord	Traversing Roots
1	1876	Gowers [9]	..	.....	.....	Conus	Lateral half	Anterior and posterior; posterior roots more disorganized
2	1884	Braubach [28]	F	14 mo.	4 yr.	C5 to T4	Right posterior surface	None
3	1888	Turner [23]	F	42 yr.	12 yr.	Midthoracic portion of cord	Left side	Present
4	1899	Spiller [6]	F	.....	.....	Filum terminale	.....	Present as small bundles separated by fat
5	1906	Root, E. F., cited by Bucy and Gustafson [20]	F	28 yr.	15 yr.	Midthoracic portion of cord	.....	.....
6	1912	André-Thomas and Jumentié [33]	M	.....	.....	L5 to S5	Posterior	Present
7	1913	Wolbach and Millet [7]	M	Birth (?)	10 mo.	Entire cord; cauda equina	Posterior	Present
8	1918	Oppenheim and Borchardt [10]	M	31 yr.	13 yr.	C1 to C4	Midline posterior	.....
9	1920	Ritter [18]	M	40 yr.	3½ mo.	C1 to T1	Right posterior	Present, greatly infiltrated and subdivided by fat
10	1921	Henneberg [35]	..	.....	.....	Cervical portion of cord	Midline posterior	Absent (?)
11	1925	Elsberg [24] †	F	17 yr.	5½ mo.	C8 to T2	Lateral surface, anterior to dorsal roots	None
12	1925	Elsberg [24] ‡	F	19 yr.	3 mo.	T2 to T4	Lateral surface, anterior to dorsal roots	None
13	1927	Stookey, B.: Am. J. Dis. Child. **36**: 1184-1203 (Dec.) 1928	M	1? yr.§	10 yr.	C2 to T5	Posterior; more to the right (?)	Present
14	1927	Bielschowsky and Valentin [31]	M	Birth (?)	1 yr.	T11 to S4	Posterior	Present
15	1928	Sachs and Fincher [8]	M	43 yr.	3 yr.	T7 to T8	Midline posterior	None
16	1928	Fay [27] ¶	F	21 yr.	2 mo.	T3 to T7	Posterior	Present
17	1928	Beykirch [34]	M	33 yr.	3 yr.	Cauda equina	.....	Present
18	1931	Kernohan, Woltman and Adson [14]	M	11 yr.	8 yr.	C4 to T1	Midline (?)	.....
19	1935	Eckart [29]	F	24 yr.	6 yr.	Midcervical to lumbar	.....	.....
20	1935	Stotz, in discussion on Fischer, D. W.: Zentralbl. f. Chir. **62**: 2970 (Dec. 14) 1935	..	.....	.....	.....	.....	.....
21	1936	Dobrokhotoff, cited by Jabotinski,[22] and Kouraeff, cited by Jabotinski [22]	F	24 yr.	1½ yr.	Cervical to lumbar	.....	.....
22	1936	Scherer [25]	F	40 yr.	1½ yr.	C4 to T5	Right dorsal root line	Present and widely separated by fat
23	1937	Guillain, Bertrand and Salles [26]	F	42 yr.	10 yr.	T5 to L5	Entire dorsal surface	Present and widely separated by fat
24	1938	Bucy and Gustafson [20]	M	1-2 yr.?	17 yr.	C1 to C4	Posterior	?

* This information is taken from the report by Bucy and Gustafson.[20]
† This is the sixth case of extramedullary tumor to be reported and is described on page 29 of Elsberg's book.[24]
‡ This is the eighth case of extramedullary tumor and is described on page 39 of Elsberg's book.[24]
§ A history of weakness dating back to 1915 was given to other physicians in 1919, when the patient was 3½ years of age. The patient must have been born in the latter part of 1915 and the weakness noted shortly after.

Connective Tissue	Spinal Puncture	Roentgenographic Evidence	Other Disorders	Operation
Capsule of pia; excessive fibrous tissue where tumor attached to cord; extensions into cord not prominent	.....	.....	Tabes.....	Necropsy
Proliferation of stroma with extensions into cord; increased nuclei	.....	.....	.....	Necropsy
Pia thickened and cellular; cellular fibrous tissue sending strands into cord	.....	.....	Obesity.....	Necropsy
No invasion of filum.....	.....	.....	Tabes.....	Necropsy
No extensions into cord....	.....	.....	.....	Tumor removed; improvement; death two years later, of pneumonia *
Invasion and destruction of cord by fibrous tissue	.....	.....	.....	Necropsy
Benign fibrous extensions into cord; increased vascularity	.....	.....	Intracranial lipoma; hydrocephalus; absence of right kidney; harelip	Necropsy
Lipomatous and "sarcomatous" extensions into cord	.....	.....	.....	Subtotal removal of tumor; patient still helpless
Pial septum between tumor and cord, sending cellular strands into cord; embryonic fat forming new lobules; liposarcoma (?)	.....	.....	Kyphoscoliosis; hydrocephalus	Necropsy
Lamina of connective tissue next to cord; heavy strands penetrating cord; "proliferated endothelium"	.....	.....	.....	Exploration (?); necropsy
Some of cord substance came away with tumor; some extensions into cord (?)	Fluid xanthochromic; globulin present	Kyphosis and arthritis	.....	Two stage removal; patient walking four years later
Stroma much more cellular in one photomicrograph than in the other	Fluid xanthochromic; globulin present	.....	.....	Total removal in two stages; complete recovery
Minimal amount in specimen removed	Almost complete block; fluid xanthochromic; globulin high	Spinal canal widened (C3 to T3)‖	Subcutaneous lipoma over intraspinal lesion	Partial removal; some improvement three years later, then recurrence *
Thickened pia sends heavy processes into cord	.....	.....	Hydrocephalus; hydromyelia; clubfeet; pseudohermaphroditism; cataracts	Necropsy
Dense capsule with minimal stroma	Normal fluid; steppage type of fall of pressure	Spine normal; picture after injection of iodized oil suggestive	.....	Total removal; death eight years later of unknown cause *
Tumor fibrous; superficial "invasion" of cord	Fluid xanthochromic; protein increased; no block	Spine normal	.....	Capsule incised; death in three months
Minimal stroma with few nuclei	Nonne reaction positive	Descent of iodized oil held up at T11	Conus abnormally high	Partial removal; improvement
Minimal stroma with few nuclei	Fluid xanthochromic; globulin present; slow fall of manometric pressure	.....	.....	Partial removal; complete recovery; recurrence nine years later
Fibrous regions	.....	No block to ascent of iodized poppyseed oil	.....	Necropsy
Fibrolipoma with destruction of whole thickness of cord	.....	No block to ascent of iodized poppyseed oil	.....	Necropsy
.....	Tumor diagnosed by this test, but results unknown	.....	.....	Partial removal twice with benefit; death from meningitis after third operation; necropsy
Capsule of pia; fibrous proliferation of perineurium where roots enter cord	.....	Spine normal	.....	Necropsy
Fibrous tissue infiltrated and dorsal columns destroyed	220 mg. of protein per 100 cc.	.....	.....	Necropsy
Dense capsule; light stroma	Albumin content normal; reaction for globulin positive; no block	Spinal canal widened from C1 to C3; complete block (to ascent) of iodized poppyseed oil at C4	Umbilical hernia; pilonidal cyst; lipoma of neck over deep lesion	Subtotal removal; excellent result

‖ The roentgenogram included in the definitive report shows widening of the vertebral canal from at least the fifth cervical to the third thoracic vertebra. In another paper (1928) a different roentgenogram is shown, in which the pedicles are shown to be affected as high as the third cervical vertebra.

¶ This is apparently the same case as that reported in more detail by Wilson, Bartle and Dean,[43] though they did not indicate this.

	Year	Author	Sex	Age at Onset of Symptoms	Duration	Level	Position on Cord	Traversing Roots
25	1938	Baker and Adams [20]	F	Birth (?)	1 yr.	Entire cord	Posterior	?
26	1939	Jabotinski [22]	F	3 mo.	13 yr.	C1 to C8	Left dorsal surface	Present
27	1944	Case 2, this series	F	19 yr.	1 yr.	T7 to T11	Posterior	Present and widely separated by fat
28	1944	Case 3, this series	M	41 yr.	2 yr.	T9 to T10	Right dorsal roots	Hypertrophic and disorganized
29	1944	Case 4, this series	M	18 yr.	4 yr.	T6 to beyond C7	Right posterior (?)	.....

was described by Gowers. In the collected cases and in the case reports to follow there is no instance of spina bifida.

Because of the special causation of lipomas in the intradural region occasioned by the paucity of fat in this location, as contrasted with lipomas in the extradural situation, where fat is abundant, because of the structures within the dura likely to become involved in the tumor while this membrane obviates such a possibility in the case of tumors outside it and because it is the classic practice to make the separation of intradural and extradural tumors the first step in clinical classification, the intradural lipomas will be considered apart from the extradural lipomas and the corresponding features of the two types will be harmonized later.

INTRADURAL LIPOMA

The total number of cases of intradural lipoma reported in narrative form is only 26. An additional 10 or 12 cases have been merely tabulated in reports of series of tumors. Table 1 lists in chronologic order the cases previously recorded, together with the cases reported in this paper. The essential features of each case may be gathered from table 1, without the necessity of our giving a narrative description of each one.

Frazier and Allen [10] tabulated 4 cases of intraspinal lipoma, in 2 of which the growth was intramedullary in the cervical region and operation was performed, occurring in a series including cases from the literature and personal cases as of May 1915 (according to Steinke,[4] who collected the cases and made a separate report). Since no such cases had been reported by other authors prior to this publication, these 2 cases must have occurred in the personal experience of Frazier and Allen and never have been reported elsewhere. Since nothing is known of these cases, they are not included in the tabulation.

Von Lennep [5] had 1 instance of intradural lipoma among the cases which he reported in tabular form, but he gave no details and we do not include it.

Schmieden and Peiper [11] described an intramedullary tumor of the spinal cord which other authors have accepted as a lipoma but which will not be so considered here. The tumor was devoid of pial connection, was soft but solid and had the gross appearance of adrenal gland tissue. When it was cut across, multiple minute bleeding points were observable on the cut surface. It consisted of densely packed round and oval cells containing many small droplets of doubly refractile fat and was stated to be a lipoblastoma. It is our opinion that the true nature and proper designation of this lesion was hemangioendothelioma. The tumor did not contain adult fat cells—only cells with fat in droplets, which are seen so abundantly as the "pseudoxanthoma cells" of hemangioendothelioma. The multiple bleeding points, caused by release of the blood contained within the small blood spaces of the hemangioendothelioma, are characteristic of such a tumor.

According to Antoni,[12] Foerster stated in a personal communication that he had encountered 3 cases of intramedullary lipoma, but no details are known.

10. Frazier, C. H., and Allen, A. R.: Surgery of the Spine and Spinal Cord, New York, D. Appleton and Company, 1918.

11. Schmieden, V., and Peiper, H.: Ueber ein erfolgreich operiertes endomedulläres Lipom des Halsmarks, nebst einigen Bemerkungen zur Chirurgie der intramedullären Tumoren, Deutsche med. Wchnschr. **55:** 513-516 (March 29) 1929.

12. Antoni, N.: Tumoren des Rückenmarks, seiner Wurzeln und Häute, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 14, pp. 1-131.

Cases of Intradural Lipomas—Continued

Connective Tissue	Spinal Puncture	Roentgenographic Evidence	Other Disorders	Operation
Dense membrane separating tumor from cord; some small and actively growing cells	.....	.....	Absence of iris; hydrocephalus; intracranial lipoma; defect of left temporal bone; xanthoma of eyelids	Necropsy
Fibrous tissue proliferated and sending extensions into cord	.....	.....	.....	Necropsy
Connective tissue of roots hyperplastic at dorsal root origin; extensions into cord	120 Gm. of protein per 100 cc.; no block	Left pedicles from T5 to T9 thinned; backs of bodies of vertebrae T6 to T8 eroded	.....	Partial removal; no improvement
Heavy septums bearing roots	100 mg. of protein per 100 cc.; no block	Pedicles of T11 eroded; descent of iodized oil obstructed at T10	Obesity; pilonidal cyst; extradural lipoma on right root at T9	Total removal
Lipoma slightly fibrous....	120 mg. of protein per 100 cc.; 11 cells per cu. mm.; partial block	Pedicles of vertebrae T3 and T4 eroded; more on right side than on left	.....	Laminectomy without removal

Jaeger[13] appears to have reported a case recently, since a title suggestive of such an observation is listed in the *Quarterly Cumulative Index Medicus*. The foreign journal in which Jaeger's paper appeared no longer reaches the Mayo Clinic library, however.

Additional data on 4 cases of intradural lipoma observed at the Mayo Clinic (cases 18, 27, 28 and 29, of table 1) are given in the following paragraphs.

REPORT OF CASES

CASE 1.—A Jewish youth aged 19 years registered at the clinic on July 10, 1927, complaining of numbness of the legs and the left hand, weakness of the arms and legs, pain in the neck and difficulty with urination. This case was mentioned previously by Kernohan, Woltman and Adson[14] and by Adson.[15]

The family history was of no consequence, but the previous medical history was of possible significance. At the age of 5 or 6 years the patient had fallen down a flight of twenty-four steps and injured his neck in an unspecified manner. Gradually increasing low cervical pain followed this injury. Cervical traction for six months had given relief, and a brace to the neck was worn for the next year. At the age of 8 years a bone graft had been performed on the cervical portion of the spinal column for what was stated to be tuberculosis.

A three or four year period of fair health followed, and it was not until the age of 11 or 12 that neurologic symptoms began. The first sign noted was clumsiness in walking, and it was thought at the time that the left leg was most affected. After an unspecified time the legs began to drag and the arms became weak. A year later there was onset of a recurring low cervical pain, which lasted only a month or so out of the year, but appeared yearly for six years. Three months before the patient came to the clinic the pain had begun again but failed to disappear as before. This pain was usually a dull ache over the low cervical spinous processes, with occasional extension to the left shoulder, but sometimes it was throbbing. At the age of 15 years the weakened arms became awkward. At the age of 18 atrophy of the hands was noted, the right leg became much weaker at the hip and numbness was felt from the waist down. In March 1927 some sort of operation had been performed on the neck, without influencing the course of the disease. During the month preceding the patient's registration at the clinic numbness of the fingers of the left hand and a rapid increase of all symptoms developed, together with difficulty in starting the flow of urine.

The physical examination, aside from the neurologic portion, gave essentially normal results. The patient walked with a spastic gait. Below the second thoracic dermatome there was total absence of appreciation of painful, thermal, tactile, joint and vibratory stimuli except that the back of the left thigh and calf retained slight cutaneous sensibility. Joint and vibratory sensibilities were diminished slightly in the hands, and there was moderate diminution of appreciation of pain and touch in the ulnar distribution of both hands. Considerable weakness of the finger flexors and the intrinsic muscles of the hand was apparent, being more severe on the left side. The legs were weak and spastic. The biceps reflex was normal, but the triceps reflex was notably diminished on both sides. A Hoffmann sign was elicited on the left side. The patellar and achilles reflexes were exaggerated, being stronger on the right side than on the left. The presence of ankle clonus and the Babinski sign bilaterally completed the picture.

Lumbar puncture revealed xanthochromic fluid, in which there was globulin. The manometric rise on jugular compression was normal, but the fall was slow.

On July 20, 1927 laminectomy of the third cervical to the first thoracic vertebrae was performed. A fusiform intradural swelling was immediately noted. After the dural opening was made, the swelling was observed to be a yellowish tumor fixed to, and lying on, the back of the cord. It measured 12 cm. in length and 3 cm. in breadth. A sagittal incision of this mass was cautiously made, and the impression was gained that the entire depth of the cord was involved. A V-shaped strip was longitudinally excised, and the incision was closed.

No change occurred during the short period of postoperative observation, during which time two roentgen ray treatments were given over the tumor. In a letter

13. Jaeger, F.: Ueber Lipome der hinteren Schliessungslinie, Zentralbl. f. Chir. **68**:2-6 (Jan. 4) 1941.

14. Kernohan, J. W.; Woltman, H. W., and Adson, A. W.: Intramedullary Tumors of the Spinal Cord: A Review of Fifty-One Cases, with an Attempt at Histologic Classification, Arch. Neurol. & Psychiat. **25**:679-699 (April) 1931.

15. Adson, A. W.: Intraspinal Tumors: Surgical Consideration, Internat. Abstr. Surg. **67**:225-237 (Sept.) 1938.

received from the patient in October 1927 rapid improvement was reported. In 1942 we were informed [16] that since the letter of 1927 the patient had made a complete recovery and had become the sectional tennis champion, but that for six or seven years prior to 1942 his arms and legs had been becoming weaker.

The tissue removed consisted entirely of adult adipose tissue. Delicate fibrous septums divided the fatty mass. Blood vessels were sparse, and no nerve tissue, either cord or roots, appeared in the surgical specimen.

CASE 2.—An unmarried white woman aged 20 registered at the clinic on Jan. 30, 1935, complaining of pain in the back, numbness of the legs and weakness of the left leg. These symptoms had appeared after a recent injury.

The only item of importance in the medical and family history concerned the father, who had diabetes. The patient stated that she had been well in every respect until March 3, 1934, when she was struck in the abdomen by a cash register, which slipped from the hands of a fellow employee as it was being carried past her. The blow forced her back against the horizontal edge of a counter. A few hours later the back began to pain, and the next day pain appeared in the toes of the left foot. Two days later the pain ascended the left leg in a vague fashion, the toes of the left foot became numb and she tripped when she was climbing stairs. Both the pain in the leg and that in the back were made worse when she reclined and were ameliorated when she sat or walked. On March 10, 1934 girdle pain over an area, a handbreadth in width, developed about the abdomen. A week later a limp was noted. Ten days later the left thigh was involved in the numbness, previously limited to the toes. The next day the right ankle was painful, and a week later numbness became apparent in the right thigh. On April 8 a physician who had been consulted found analgesia below the waist. Sensation was almost entirely regained during the next eight weeks, and no progression was noted until September 1934, when the left leg was observed to be atrophic.

A lumbar puncture, performed on Oct. 16, 1934, revealed that the manometric readings were normal. The patient's blood pressure was noted to be elevated at about this time. During the first part of December the pain in the back had become much worse and had required administration of an unidentified medicament for relief. In January 1935 roentgenographic examination of the spinal column had led to a diagnosis of tumor of the spinal cord.

Physical examination revealed nothing abnormal except in the nervous system. Sensation was normal above the ninth thoracic dermatome, but there were complicated sensory changes below this level. Appreciation of touch and temperature was absent over the right lower quadrant of the abdomen and the right thigh and was greatly diminished over the left side of the abdomen, the left thigh and the lower part of the right leg and foot. The lower part of the left leg and foot displayed minimal hypesthesia and hypalgesia. Vibratory and joint sensibilities were absent over the right ankle and were diminished over the left one. The entire left leg was moderately weakened, but the right leg was of normal strength. The hamstring reflexes were increased

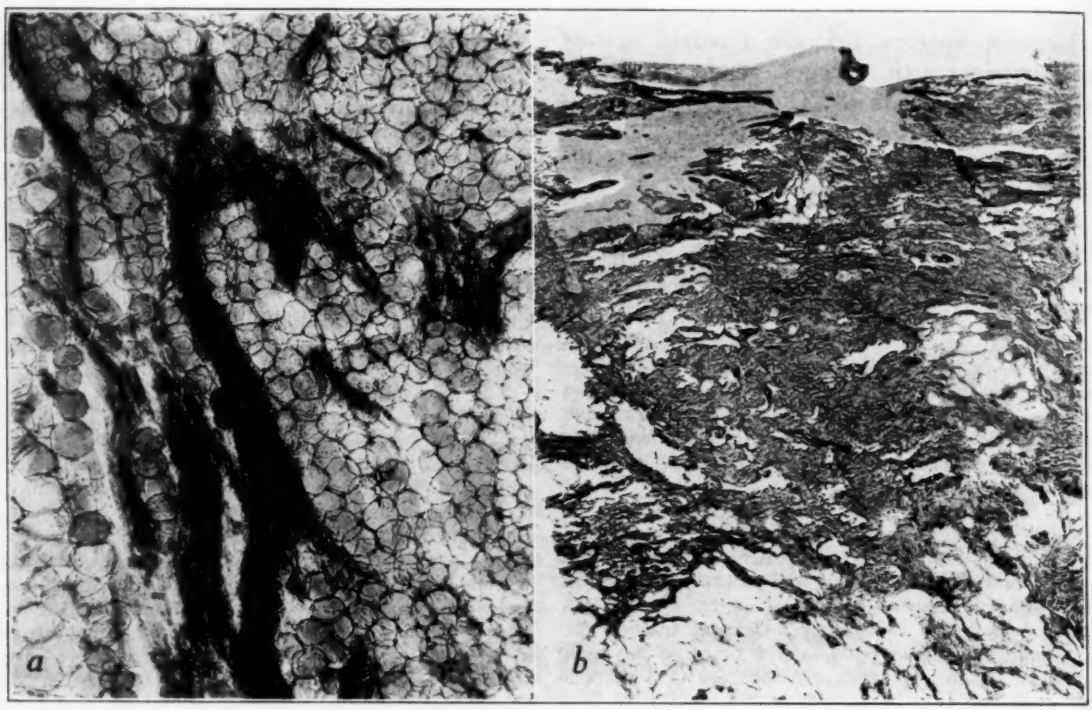

Fig. 1 (case 2).—(*a*) Fine bundles of root fibers traversing the lipoma (sudan III and hematoxylin; × 45). Note how intimately the root structure is infiltrated by the fat despite the absence of active-appearing tissue. (*b*) Fibrocellular tissue separating the fat from the cord. (Perdrau stain; × 20). Note the heavy extensions into the neural tissue at the top and how strands of neural tissue become sequestered (left center); also note the occurrence of islets of fat within this tissue.

16. Adelstein, L.: Personal communication.

on the left side, but the patellar and achilles reflexes, though moderately hyperactive, were of equal strength on the two sides. There were mild clonus of the left ankle and a Babinski sign bilaterally. The abdominal reflexes were absent.

Roentgenographic examination of the thorax revealed enlargement of the heart. Examination of the spine disclosed thinning of the pedicles of the fifth to the ninth thoracic vertebrae inclusive and erosion of the backs of the fifth to the eighth thoracic vertebrae. The spinal canal was much widened in this region. Lumbar puncture revealed an initial pressure of 10 cm. of fluid. This rose to 14 cm. after ten seconds of bilateral jugular compression and promptly fell back to the initial pressure on release. The Nonne test gave positive results, and the total protein content measured 120 mg. per hundred cubic centimeters of cerebrospinal fluid.

1943. She no longer uses crutches but is able to walk long distances with a cane. She is able to raise each foot off the ground to a distance of 12 inches (30 cm.), but is unable to jump at all. Clonus causes embarrassment if the foot is not properly supported. She is working in a self-supporting occupation.

The surgical specimen consisted of a longitudinal strip of the tumor, which included a small amount of the posterior columns of the cord on its anterior surface and permitted of accurate study of the relation of the tumor to the cord. The greater portion of the tumor was composed of typical adult adipose tissue. The free surface of the mass, the portion lying exposed on the posterior surface of the cord, was ensheathed by a fibrous capsule of moderate thickness, which in some places consisted of an outer layer, with the collagenous fibers running in a vertical direction, and an inner layer, with

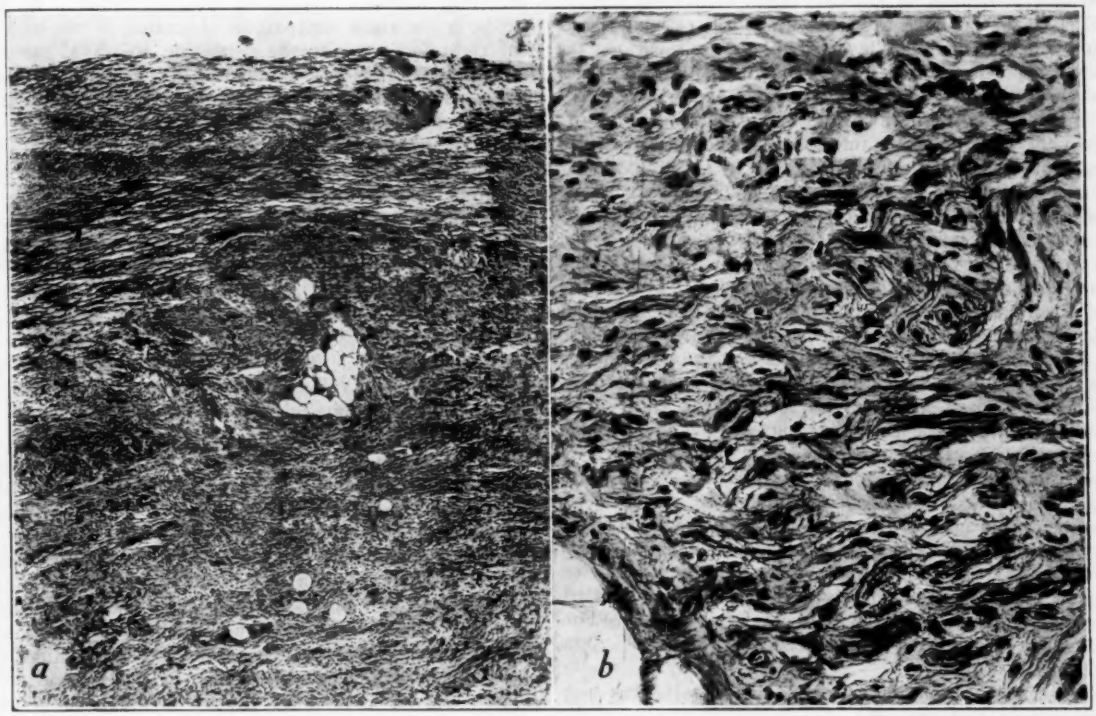

Fig. 2 (case 2).—Fibrocellular tissue separating the fat from the neural tissue. (*a*) The neural tissue at the top of the section is infiltrated by heavy strands, while the mass of tissue in the lower portion of the field shows scattered development of adipose tissue (hematoxylin and eosin stain; × 32). (*b*) Higher power of an area off the upper right corner of the islet of fat in the center of *a*. The Mallory-Heidenhain preparations of parts of this tissue showed roots contributing to the tangle (hematoxylin and eosin stain; × 215).

On Feb. 5, 1935 laminectomy of the fifth to the ninth thoracic vertebrae was performed. The bone was thin and excessively vascular. When the distended dura was opened, a large tumor on the posterior surface of the cord was exposed. This could not be separated from the cord, and a V-shaped longitudinal strip was taken from the most prominent meridian.

For three days the patient was paraplegic, but by the twentieth day she was able to stand and had control of her bladder. The right leg was analgesic, but the left leg showed only minimal hypalgesia. Vibratory sensibility was notably diminished on the right ankle but only moderately so on the left ankle.

By 1937 the patient was using crutches to get about and was able to take a few steps alone. A letter has been received describing her condition as of August

the fibers running in a horizontal direction around the tumor. The fibrocytic nuclei usually present in a capsule of this type were normally sparse. In some places numbers of small vessels were present immediately subjacent to the inner layer of this capsule, but on the whole the vascularity was not remarkable. The adipose tissue beneath the capsule did not contain any embryonic fat or active-appearing tissue.

As the interior of the tumor was approached from the capsular surface, one began to encounter small bundles of nerve fibers cut transversely, obliquely and longitudinally, all in the same section. These bundles had the undulating course and the connective tissue sheaths characteristic of peripheral nerves and must, therefore, be considered as rootlets traversing the tumor. The sections stained for fat showed beautifully these root-

lets coursing through a galaxy of red spherules (fig. 1*a*). The bundles of nerve fibers were mostly small and some of them contained only a few individual fibers. All the interstices were filled with fat, and the impression was gained that the fat had its origin from some structure originally lying within the root and bearing an intimate relation to its individual fibers. In other locations the rootlets lay in a moderately delicate stroma composed of anastomosing strands of fine collagenous fibers and cleftlike spaces, in which lay acidophilic granules in clumps. The only nuclei were pyknotic spindles, looking like the nuclei of fibrocytes, lying mostly in close association with the collagenous strands but sometimes seeming to be free in the clefts. The most adequate interpretation of this stroma is that it was myxomatous.

As the surface of attachment to the cord was approached, the amount of adipose tissue was diminished by heavy strands of cellular tissue extending into it. Finally, the fat gave way entirely to this cellular tissue, and a heavy, irregular layer of this tissue separated the adipose portion of the tumor from the neural substance of the cord. On the face of this separating layer next the cord one first saw sequestered islands of cord; then the cord tissue became prominent and was invaded by heavy strands passing into it (fig. 1*b*). This cellular tissue was composed of a tangled collagenous network bearing a variety of cells (fig. 2). Most of the cells were oval or spindle shaped, vesicular or pyknotic, and were certainly of connective tissue origin. Even in this tangle of fibers orientation was apparent. The course of the fibers was roughly parallel with the course of the nerve fibers in the white matter of the spinal cord.

No giant cells or mitotic figures were present in this tissue despite its superficial resemblance to sarcoma. No fat lay bare within or adjacent to the cord. The little fat within the cord was enclosed by the cellular connective tissue; in other words, fat was present in small amounts in the fibrous extensions from the septum into the cord. The Mallory-Heidenhain preparations revealed this cellular tissue to be of radicular origin. Lying between the dense, blue-stained collagenous fibers were faintly orange myelin tubules. The intraradicular connective tissue (endoneurium) had all but obliterated the nerve fibers, so strongly hyperplastic was it. The vascularity of this cellular connective tissue was minimal.

In certain sections in which the hyperplasia was less conspicuous and one was able to follow the roots to their entrance into the cord the roots were disrupted and distended with fat cells, so that the fat cells were partitioned one from another by septums bearing single layers of myelinated nerve fibers. Sections cut transversely across the tumor showed root fiber bundles and isolated individual myelinated nerve fibers closely applied to the cord in the septum separating the tumor from the cord; these roots were distributed over an unnaturally large portion of the circumference of the cord. Whereas posterior roots normally enter the cord along the posterolateral sulcus in a zone 1 or 2 mm. wide, in some locations the tumor roots were present in the septum over a segment of the circumference of the cord 1 cm. wide. Furthermore, these roots were cut transversely just as were the fibers of the cord.

CASE 3.—A man aged 41 registered at the clinic on Oct. 7, 1935, complaining of a burning sensation in the toes of the right foot and numbness, weakness and cramps of the right leg.

The patient's family history was noncontributory except that he had had a sister who had been obese before her death, of unknown cause, at the age of 50 years. The previous medical history is of interest. A pilonidal cyst had been operated on in 1928. In 1930 the patient had a gastric hemorrhage. In 1932 he injured his back in a fall and was confined to bed for a month. He was otherwise well, though obese, until March 1935, when there appeared a burning pain in the toes of the right foot and some acral numbness. During the next seven months this numbness gradually and unremittingly ascended the leg to the groin. A month after the onset of the burning the patient had noted weakness in the right leg, associated with twitching and cramping of the muscles of this leg.

The patient was obese, but the general physical examination did not reveal anything else significant. Positive findings elicited by the neurologic examination included moderate diminution of joint and vibratory sensibilities in the right leg and minimal diminution in the left leg, minimal hypalgesia and hypesthesia to the groin in the right leg, paresis of motion of the toes of the right foot, and, on the same side, increased patellar and achilles reflexes, a diminished hypogastric reflex, an ankle clonus and a Babinski and related toe signs. Lumbar puncture revealed colorless fluid and absence of block. However, the total protein amounted to 100 mg. per hundred cubic centimeters of cerebrospinal fluid, and the reaction for globulin was positive.

The patient was not seen again until February 1938, when he stated that the cramping had diminished but that the toes of the left foot had begun to burn during the previous November. The right leg tired greatly after he walked a few blocks, and a pain was present over the right lumbosacral area, which was made worse by his reclining on the right side and was relieved by his walking about. This pain was not exaggerated by coughing or sneezing.

Examination at this time showed progression of neurologic disturbance. The vibratory and joint senses were absent in the right leg and were moderately diminished in the left leg. There was hypalgesia over the left side of the sacrum, the posterior aspect of the left thigh and the left foot. Perception of pain in the right leg was normal. The entire right leg was moderately weakened and exhibited increased reflexes and clonus. The hypogastric reflex was almost absent on the right side, and there was a Babinski sign bilaterally.

Myelography, with radiopaque oil, performed on March 1, 1938, revealed partial obstruction to the descent of the cisternally injected oil at the lower part of the tenth thoracic vertebra. The lower end of the obstructing mass lay in the middle of the eleventh thoracic vertebra. Erosion of the pedicles of the eleventh vertebra was noted in these myelograms.

Laminectomy of the tenth and eleventh thoracic vertebrae, performed on March 4, 1938, revealed a yellow intradural tumor lying on the right posterior aspect of the spinal cord, intimately attached to several root filaments at their emergence from the cord and possibly involving the cord itself. The incision was widened to the right to effect removal of this tumor, and another tumor, extradural in location, was encountered on the ninth thoracic root. The second tumor was entirely separate from the larger, intradural tumor and did not occur on the same root, lying, as it did, on the root above. Both tumors were removed under the impression that they were neurofibromas. The cord was compressed by the intradural tumor to about one-third normal size.

On the seventeenth postoperative day there was still weakness in the right leg. The Babinski sign was not present on the left side, but ankle clonus, stronger on the right side than on the left, was elicited. Joint and

vibratory senses had returned to normal. There was absence of appreciation of touch, pain and temperature over the right lower quadrant of the abdomen and the front of the right thigh. On the patient's return to the clinic, on Aug. 25, 1938, he stated that he had been getting about with a cane until three weeks prior to this date, when he was caused to fall by his right leg's jerking involuntarily into flexion. The legs tired more easily and felt stiffer after this episode than they had before. Cramping began in the right calf. The left leg would involuntarily flex when the patient was in bed. Perineal numbness was noted at stool. Examination showed considerable weakness of the hamstring muscles and the muscles of the calf, moderate weakness of the quadriceps and minimal weakness of the psoas and gluteal muscles, all on the right side. The left leg was strong. Both legs exhibited increased tone. Ankle clonus and increased tendon reflexes were present on the right side. A Babinski sign was elicited on each side. Joint and vibratory senses were absent in both legs to the knees. Cutaneous sensibility was diminished below the tenth thoracic dermatome and was absent below the knees. Roentgenographic examination showed only absence of the laminas which had been removed. A lumbar puncture yielded colorless fluid, containing 55 mg. of protein per hundred cubic centimeters. There was no block. Further surgical treatment was not advised. The patient has not responded to our recent inquiry, and his present status is unknown.

The intradural tumor consisted of adult adipose tissue, traversed by heavy fibrous septums bearing bundles of root fibers. At the extremity of some of these fibrous septums there was present glial tissue similar to that in the white matter of the spinal cord. In some regions the rootlets to this glial segment were considerably disorganized and lay in the fibrous stroma in small bundles separated by heavy collagenous bands and small groups of fat cells. In another septum a single large root was almost the sole occupant. In one location this root became a tangled mass of hyperplastic endoneurium, which merged imperceptibly with the surrounding heavier collagen strands at the periphery and was not separated from the surrounding tissue by a condensed band of connective tissue. Small amounts of fat lay within the fibrous septums, but no fat was present within the hyperplastic root. Almost all the fat lay in the lobules between the root-bearing septums. The vessels of this tumor were scanty. Tissue from the extradural tumor is no longer available.

Case 4.—The patient presented himself at the clinic in September 1943, complaining of pains in the back, the thorax and the right leg. He was 22 years of age, single and a farmer.

The family history was without significance. The patient had been well until four years prior to his coming to the clinic, when he became jaundiced for two weeks and was put to bed. The first day out of bed, after the jaundice subsided, he carried a quantity of lumber from the basement and the following day had a sore back, which caused him to walk bent over. Shortly after this the right leg felt stiff and seemed to drag. A certain degree of recovery occurred, but during the year prior to registration at the clinic the patient was bothered by bouts of pain in the right leg, which lasted about two hours and were followed by weakness in the leg. In August 1943 soreness reappeared in the upper part of the back, and the pain seemed to run into the left side of the thorax. There was a spot in the midthoracic segment of the spinal column which pained on walking. Coughing and sneezing caused pain in the midthoracic region of the back and around the lower part of the sternum. A pain appeared in the right thigh whenever the patient exercised. His temperature had been 100 F. since August.

The patient was well built and seemingly well; he appeared moody and was perhaps less bothered by his pains than he asserted. The general physical examination revealed nothing of significance except for a low grade fever. The neurologic examination revealed only that the left pupil was larger than the right, and the vibratory and joint sensibilities were diminished in the lower extremities.

Routine examination of the blood, flocculation tests and urinalysis gave normal results. Roentgenograms of the spinal column showed erosion of the inner margins of the pedicles of the second and third thoracic vertebrae, particularly of the right pedicle of the third vertebra. Spinal puncture was performed on September 18. The initial pressure was 15 cm. of fluid. On jugular compression the pressure rose to 19 cm. of fluid. The fall was slow. Ten cubic centimeters of the colorless fluid was removed, and the final pressure was 1 cm. The fluid contained 11 cells per cubic millimeter, small amounts of globulin and 120 mg. of total protein per hundred cubic centimeters.

Myelography, with the use of radiopaque oil, was performed on September 22. There was almost complete obstruction to the passage of the oil upward at the fourth thoracic interspace. This deformity was mostly on the right side and was interpreted as being due to an intradural extramedullary tumor. Later the same day laminectomy of the fifth thoracic to the seventh cervical vertebrae was performed. The distal end of the tumor lay in the lower end of the incision; but the upper pole was beyond the highest exposed segment, and the surgeon deemed it unwise to go farther, since the growth could not be separated from the cord. The tumor was yellow and had the appearance of adult fat. A small fragment was removed from the dorsal surface, and this proved to be adult adipose tissue with increased stroma.

The patient's convalescence was complicated by postoperative hematoma. After the removal of this clot gradual recovery occurred.

Clinical Features of Intradural Lipomas.—Twenty-nine cases of intradural lipoma are available for comparison and analysis. The distribution of these tumors between the sexes appears to be about equal. Fourteen patients were females; 12 were males, and the sex of 3 patients was unknown. This slight inequality at least does not run counter to the distribution between the sexes of lipomas in other locations which is given as about 3:2 in favor of females (Geschickter [17]).

Consideration of the ages at which the first symptoms began leaves one with the impression that this tumor makes its presence known only during three rather well delimited age periods: before the age of 2 or 3 years, on the patient's reaching manhood or womanhood and in early middle age. In only 4 cases did the tumor fail

17. Geschickter, C. F.: Lipoid Tumors, Am. J. Cancer **21**:617-641 (July) 1934.

to conform to this generalization. The distributions of the ages of onset are charted in figure 3. In view of what has been said by other authors and what we shall have to say regarding the probable existence of most of these tumors from before birth, it might be held that the age of onset is of little importance. On the other hand, it seems to us that the onset of symptoms due to intradural lipoma must be capable of some rational explanation having to do with increased deposition of fat at certain times of life, inter-

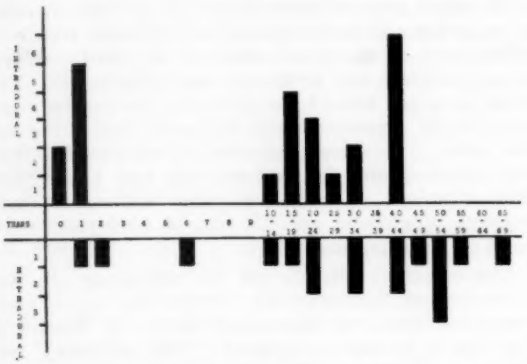

Fig. 3.—Ages at clinical onset of intraspinal lipomas. The values for the intradural lipomas are plotted above and those for the extradural lipomas are plotted below the axis of the abscissas.

ference with the blood supply to the spinal cord at a time when the vascular system begins to be less adaptable than before, edema from trauma, and perhaps other factors.

Among the cases in which trouble was experienced during the early years of life there were 3 of early death. The tumors in these 3 cases were the largest in the entire series, 2 of them extending throughout the length of the cord, and other severe defects were associated. In each of the 4 instances of early onset without early fatal termination the duration before operative intervention or death was long, being four, ten, thirteen and fifteen years, as though the trouble was due to a slowly augmenting pressure by a soft mass without infarction of the spinal cord. The tumors manifesting themselves very early, accordingly, seem accounted for on the basis of more or less massive development of a fatty mass within the dura at some time in embryonic life. In the one group this mass is very large, and other severe defects help to express the faultiness of the germ plasm or the seriousness of the factor operating in utero on the embryo and rather overshadow the intraspinal tumor with regard to the clinical picture and as a cause of death. In the other group the fatty mass is less large but so nearly fills the neural canal that it is not long in reaching such a size as to interfere with function of the spinal cord. The long history of trouble is to be considered an expression of the slow growth of the tumor and the ability of the spinal canal to accommodate it by widening. A variety of less severe developmental defects may accompany the intraspinal lesion.

The clustering of cases around the beginning of the third decade may have something to do with the filling out of the body generally, through the deposition of fat in the adipose tissue. The fact that 6 of the 7 patients in this category were females does not detract from this hypothesis. If such deposition is the correct explanation, then it is probably dependent on a nidus present before birth, as indicated previously.

The grouping of the cases in the early part of the fifth decade might be suspected to result from the final overtaking by a slowly increasing mass of a cord the vessels of which are becoming increasingly sclerotic and less and less adaptable to outside interference.

In only 1 of the cases (Ritter[18]) was the histologic picture significantly different from that of numerous other tumors of this type. In this single case there was definite evidence of new formation of fat and real activity, so that the sudden onset must be largely attributed to rapid increase in size of the tumor.

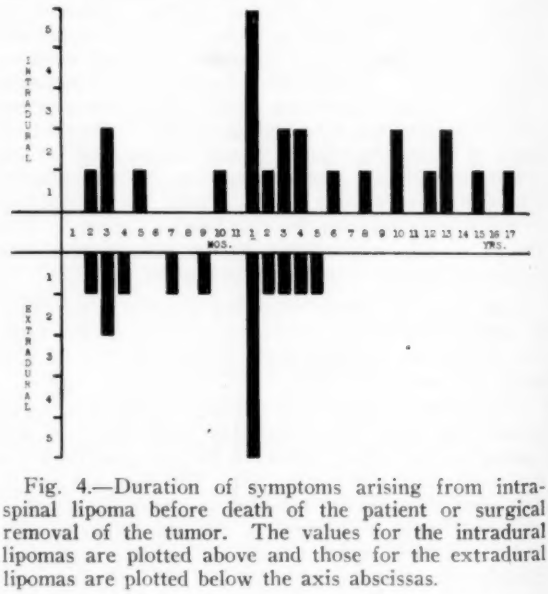

Fig. 4.—Duration of symptoms arising from intraspinal lipoma before death of the patient or surgical removal of the tumor. The values for the intradural lipomas are plotted above and those for the extradural lipomas are plotted below the axis abscissas.

Reflections on the duration of symptoms before the death of the patient or before surgical removal are rather unproductive because the terminal issues are not equivalent. Figure 4, dis-

18. Ritter, A.: Ein Lipom der Meningen des Cervicalmarks, Deutsche Ztschr. f. Chir. **152**:189-209, 1920.

playing the duration of symptoms until operation or death, is worth a moment's attention. It shows the great variation, but also indicates how in many cases, contrary to the general impression, the lipoma is of short duration. The median period is somewhere between three and four years.

The symptoms of the intradural lipomas are perhaps a little different from the symptoms of tumors of the spinal cord as a whole. Spontaneous pain, aside from painful cramp, was a prominent symptom in 10 of the 29 cases. In 3 cases (Oppenheim and Borchardt [19]; case 1 of this series; Bucy and Gustafson [20]) pain was limited to the spine. In 3 cases there was distal pain which must have been due to the tumor but was not explicable on the basis of root irritation or osseous involvement. In only 4 cases were there pains which probably were of root origin. It is clear that definite root pain is not often caused by an intradural lipoma, despite the frequent involvement of roots by the tumor. The explanation depends on the fact that this tumor is almost always so firmly fixed to the cord that the traversing roots are not pulled on when the intraspinal hydrodynamic relations suddenly shift.

An early symptom in 4 cases was awkwardness in use of the arms or legs not associated with manifest weakness. In Stookey's [21] and Bucy and Gustafson's [20] cases walking was retarded and was never normal. In the latter case the patient became unskilful in use of the hands. In case 1 of this series a maladroit gait, and then clumsiness of the arms, developed. In Jabotinski's [22] case awkwardness of the left arm was observed at the onset of the trouble.

Other symptoms were those common to all intraspinal tumors and were of no diagnostic help. Nine of the 29 cases of intradural lipoma were of no value in determining which features of the clinical examination were characteristic, if any. Many of the remaining cases are not of great value for a variety of reasons.

In 8 cases (Turner [23]; Oppenheim and Borchardt [19]; Ritter [18]; Elsberg's case VI [24]; Scherer [25]; Guillain, Bertrand and Salles [26]; cases 1 and 2 of this series) there were displayed what were essentially transverse lesions of the cord without specificity of selection of fiber tracts.

In case 3 of this series, that of a tumor of the right posterolateral region of the cord, the symptoms were about what one would expect. Appreciation of pain was diminished in the sacral dermatomes of the opposite side. Joint and vibratory appreciation was affected bilaterally, but more on the side of the tumor than on the opposite side. Abnormal reflexes were present in both legs, but only the right leg was weakened. The absence of sensory change in the dermatome served by the affected segment and root of the cord is explained by the slight linear extent of the portion of the cord affected and by overlap from adjacent dermatomes.

Before lumbar puncture Elsberg's [24] patient (case 8) had only spastic paraplegia, which was worse on the side on which the tumor lay than on the other side. After the puncture total anesthesia developed up to the fourth thoracic dermatome. The patient of Bucy and Gustafson [20] was tetraparetic, hypesthetic below the clavicles, insensitive to joint motion and vibration in the legs and hyposensitive in the arms to these modalities, but he had no disturbance of appreciation of pain or temperature. The most severe disturbance, the loss of joint and vibratory sense, was in accord with the position of the tumor on the posterior surface of the cord. Fay's [27] patient had spastic paraparesis and impaired vibratory and position sense in the legs until a lumbar puncture was done. Then the vibratory and position defect increased, and the appreciation of pain and temperature became impaired below the sixth thoracic segment, a dissociation the reverse of that displayed by Bucy and Gustafson's patient. Stookey's [21] patient had spastic paralysis of the

19. Oppenheim, H., and Borchardt, M.: Weiterer Beitrag zur Erkennung und Behandlung der Rückenmarksgeschwülste, Deutsche Ztschr. f. Nervenh. **60**: 1-31, 1918.

20. Bucy, P. C., and Gustafson, W. A.: Intradural Lipoma of the Spinal Cord, Zentralbl. f. Neurochir. **3**: 341-348 (Jan.) 1939.

21. Stookey, B.: Intradural Spinal Lipoma: Report of a Case and Symptoms for Ten Years in a Child Aged Eleven; Review of the Literature, Arch. Neurol. & Psychiat. **18**:16-43 (July) 1927.

22. Jabotinski, J.: Fibrolipome intradural de la moelle, Rev. neurol. **72**:15-31 (July) 1939.

23. Turner, F. C.: Lipomatous Tumor (? Sarcoma) of the Spinal Cord, Tr. Path. Soc. London **39**:25-27, 1888.

24. Elsberg, C. A.: Tumors of the Spinal Cord and the Symptoms of Irritation and Compression of the Spinal Cord and Nerve Roots: Pathology, Symptomatology, Diagnosis and Treatment, New York, Paul B. Hoeber, 1925.

25. Scherer, E.: Die extramedullären pialen Lipome an der hinteren Wurzellinie des Rückenmarks (Kasuistischer Beitrag), Ztschr. f. d. ges. Neurol. u. Psychiat. **154**:507-520, 1936.

26. Guillain, G.; Bertrand, I., and Salles, P.: Les lipomes spinaux intra-duraux, Ann. de méd. **42**:119-131 (June) 1937.

27. Fay, T.: Vasomotor and Pilomotor Manifestations: Their Localizing Value in Tumors and Lesions of the Spinal Cord; a Report of Thirteen Verified Cases, Arch. Neurol. & Psychiat. **19**:31-46 (Jan.) 1928.

legs, flaccid paralysis of the arms, absence of vibratory appreciation in the legs and disturbance of pain and touch appreciation from the fourth dermatome on the left side only.

Braubach's [28] patient was too young and too sick for satisfactory sensory examination, but she had hypesthesia and hypalgesia in the arms and legs and paralysis of the right arm and of both legs. It is remarkable, and of some significance, that the right arm was palsied while the left remained unaffected. The large tumor involved the segments of the cord giving rise to the brachial plexus and lay on the same side as the paralyzed arm. While the roots lay anterior to the tumor, the unilateral palsy is best explained on the basis of destruction of the roots by stretching (?), rather than of compression of the anterior horn, and the paralysis must have been of the lower motor neuron type. Scherer's [25] patient had a palsied arm from a tumor in a similar location, but in this instance the mass enclosed many roots. The same speculations apply to Scherer's case as to Braubach's; and if these 2 instance of paralysis of the homolateral arm may be explained as has been suggested, this feature is unique to lipoma. No other single tumor possesses sufficient linear extent to implicate enough roots to cause paralysis of the arm as a whole. Other tumors may of course be of considerable linear extent, but the paralysis is bilateral because it is due to compression or destruction of the anterior horn and both sides are affected.

Painful flexion of the neck and tenderness of the spinal column were observed in a few cases, but these features in no wise help to distinguish lipoma from other intraspinal tumors. Anisocoria was present in a few cases of cervical tumor, and in the 1 case in which the relations of the tumor were accurately established (Jabotinski [22]) the tumor lay on the side of the miotic pupil, as is to be expected.

Spinal puncture was performed in 13 of the 29 cases of intradural lipoma. In 5 cases the report failed to mention the results of the manometric study. In 3 of the 8 remaining cases there was no hydrodynamic block; in 4 cases there was partial block, and in 1 case, almost complete block. The cerebrospinal fluid was abnormal in each case in which block was absent. In 1 case only the reaction for globulin was positive; in the second case the total protein amounted to 100 mg. per hundred cubic centimeters of fluid, and in the third case the fluid was xanthochromic and contained increased protein. In this case the initial pressure was zero, but jugular compression caused a prompt rise to 10 cm. of fluid. Release of the compression was followed by a prompt return to zero. Significantly, this manipulation caused pain to appear in the thorax —pain such as was one of the patient's presenting symptoms. In 1 of the 4 cases in which there was partial block the fluid was normal. In this case the evidence of block was a rapid, but steppage, type of fall of fluid pressure. In 2 cases in which there was partial block the total protein amounted to 120 mg. per hundred cubic centimeters of fluid. In the fourth case the fluid was xanthochromic and globulin was present, but the total protein content was not reported. In the case of complete block the fluid was yellow and contained large amounts of globulin. In 2 of the 5 cases in which no manometric data were reported the cerebrospinal fluid was yellow and contained globulin; in 1 case it contained globulin; in 1 case it was diagnostic of tumor of the spinal cord, in an unspecified manner, and in 1 case it was reported to contain 220 mg. of total protein per hundred cubic centimeters.

The series is too small to enable one to relate the size of the tumor to the degree of block. The noteworthy circumstance is the failure of total block in at least 4 instances (Bucy and Gustafson's [20] case; cases 1, 2 and 4 of this series), in which the tumors were of such size as literally to dwarf the usual extramedullary block-producing tumor. The lipomas are somewhat similar to true intramedullary tumors in their effects on the pathway of the spinal fluid. They produce a fusiform enlargement of the cord and expand ever so slowly. They do not kink the spinal cord by pressing on it at one spot or completely fill the subarachnoid space in one small region; rather, they run to considerable length and leave the pathway stenosed but open. The presence of normal fluid in but 1 of 13 cases, and this in the case of a very small tumor which altered the hydrodynamic relations of the spinal fluid, attests the tendency to discoverable encroachment, if not obstruction.

Roentgenograms or myelograms or both were made in 14 of the 29 cases. In 5 instances localized widening of the spinal canal by erosion of the vertebral body or pedicles was noted; in 1 instance the interpretation was kyphosis and arthritis; in 4 instances the spinal column was normal, and in 4 instances the report of the myelogram did not include mention of the bony changes, if any. The tumors associated with bony changes were not significantly larger than the tumors associated with a spinal column which was reported as normal. Indeed, one of the small-

28. Braubach, M.: Ein Fall von Lipombildung der Rückenmarkshäute, Arch. f. Psychiat. **15**:489-495, 1884.

est tumors of the series (case 3 of this series) caused erosion of one pedicle. Neither did the age of onset or the duration of symptoms seem to bear any relation to the presence of bony changes. In Stookey's [21] case, however, in which there was the most extraordinary widening of the canal, the onset of the trouble appeared at a very early age. It is probable that if more roentgenographic studies were reported a case could be made out for the more constant appearance of bony changes with the early onset and long duration of symptoms. In 8 cases myelographic studies were made. In 3 cases there was complete or almost complete obstruction; in 2 cases, partial obstruction, and in 1 case, indication of tumor of an unspecified nature; in 1 case the results were unknown, and in 1 case (Eckart [29]) there was no evidence of any obstruction, although the tumor was of great linear extent.

Other physical defects were rather commonly associated with the lipomas. Extreme instances of such an association are the cases of Wolbach and Millet,[7] of Baker and Adams [30] and of Bielschowsky and Valentin,[31] in which the defects were too numerous and too obscurely related for one to say much except to classify the lesions as "multiple congenital anomalies." In 2 cases subcutaneous lipomas overlay the deeper lipoma, an occurrence which is immediately arresting, seeming to exceed in importance its mere application to the matter at hand to bear on the question of the derivation of the leptomeninges. It is probably of little significance that in 2 cases the patients were obese. The occurrence of pilonidal cysts in 2 cases should not cause one to interpret the lipoma in a similar embryokinetic light.

The distribution of the intradural lipomas along the length of the spinal cord is subject to some law which favors certain regions and tends to avoid others. In analysis of data on the tumors from this standpoint, we took care to translate the various data into terms of the actual level of the cord by referring to figure 54 of the 1939 edition of Ranson's [32] textbook. Although errors are unavoidable in an attempt to decide on which segments of the cord were exposed from descriptions of laminectomy incisions, the deviation is not likely to be large, and considerably more accuracy is attained than if laminectomy levels and segment levels of the cord were mingled in the making of comparisons. In 12 cases the tumor lay entirely above the seventh thoracic segment of the cord, and in 7 cases, entirely below the sixth thoracic segment; in 3 cases the tumor was small and occupied exactly the midthoracic region; in 5 cases the tumor was very long and lay both above and below the midthoracic level; in 1 case it was shorter, and in 1 case the location was not given. The only tumors involving the upper sacral segments were the 3 huge ones appearing as a feature of multiple congenital anomalies and attended by early death —not to say that the lesion of the cord was the cause of death—and the tumor reported by André-Thomas and Jumentié.[33] The most accurate manner of dealing with the problem of segmental distribution is to show graphically the

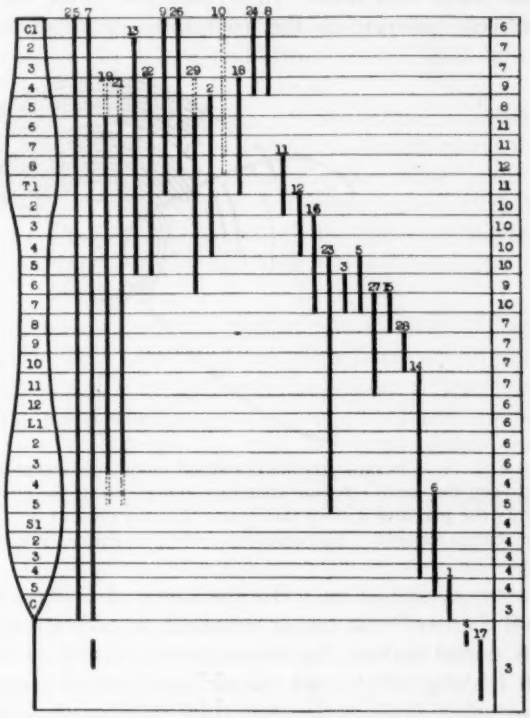

Fig. 5.—Longitudinal distribution of intradural lipomas with reference to the spinal cord. Data concerned with laminectomy and the like obtained from reports in the literature have been translated into terms of the actual segment of the cord probably involved. Pure surmises are indicated by dots. The column to the right indicates the total number of times each segment was involved by tumor. The number at the top of each tumor refers to the number of the case as listed in table 1.

29. Eckart, G., cited by Bucy and Gustafson.[20]

30. Baker, A. B., and Adams, J. M.: Lipomatosis of the Central Nervous System, Am. J. Cancer **34**:214-219 (Oct.) 1938.

31. Bielschowsky, M., and Valentin, B.: Ueber ein Lipom am Rückenmark mit Hydrosyringomyelie und anderen Missbildungen, J. f. Psychol. u. Neurol. **34**: 225-233 (Feb.) 1927.

32. Ranson, S. W.: The Anatomy of the Nervous System from the Standpoint of Development and Function, ed. 6, Philadelphia, W. B. Saunders Company, 1939.

33. André-Thomas and Jumentié, J.: Lipome du cône terminal, Rev. neurol. **20**:222 (Jan. 25) 1912.

number of times each segment of the cord is occupied by tumor (fig. 5). The lower cervical and upper thoracic region is the favorite seat of these tumors, and the conus medullaris is the most avoided region.

The distribution of the tumors around the circumference of the cord shows a predilection for certain segments of the circle and an avoidance of others. The study of this feature is attended by considerable inaccuracy, for detailed descriptions of the circumferential extent of the tumors are scarce and one must often depend on inference. Operative cases are of less value in the determination of this point than necropsy cases. Despite these reservations, the plotting of this relation to the cord brings out certain striking facts (fig. 6). In 21 cases the tumor involved the dorsal aspect of the cord between the dorsal root lines. In 6 cases the tumor was entirely anterior to the root lines or involved

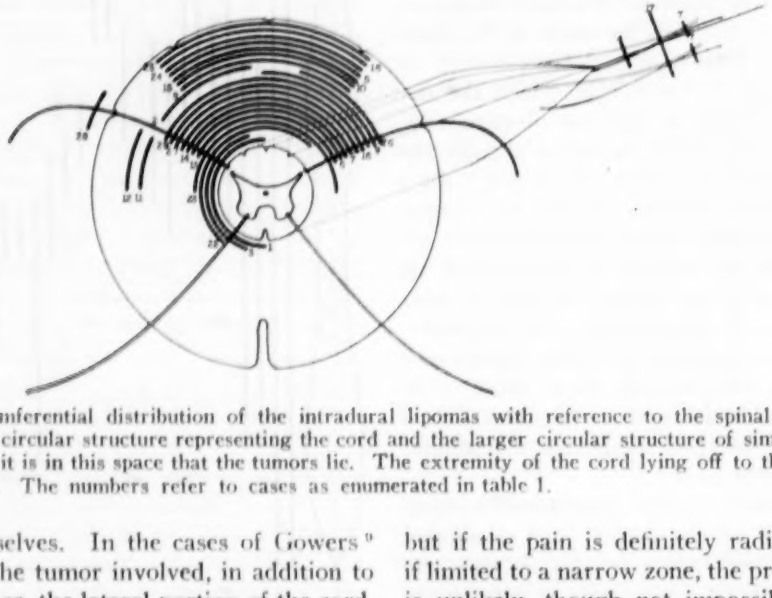

Fig. 6.—Circumferential distribution of the intradural lipomas with reference to the spinal cord. The space between the small circular structure representing the cord and the larger circular structure of similar outline represents the pia, and it is in this space that the tumors lie. The extremity of the cord lying off to the right represents the cauda equina. The numbers refer to cases as enumerated in table 1.

the roots themselves. In the cases of Gowers [9] and Turner [23] the tumor involved, in addition to the dorsal surface, the lateral portion of the cord. In Elsberg's [24] 2 cases the tumors differed from the other lipomas in that they originated just anterior to the dorsal roots and were not traversed by them. In 8 cases the tumor appeared to have arisen from the dorsal surface of the cord without incorporating roots in its substance. The state of involvement of the roots was unknown in 6 instances. In 15 of 26 cases the tumor implicated roots, and in 1 or 2 cases it probably did so; in 5 cases the tumor definitely did not involve the roots, and in 3 others it probably did not. Scherer [25] expressed the opinion that the tumor reported by him actually arose in the line of the posterior roots. Case 3 of this series is unique because of the origin of the tumor from a thoracic dorsal root alone. In the case reported by Beykirch [34] the tumor arose from the cauda equina. The tumor of the filum in the case reported by Spiller,[6] which enclosed root fibers, and the smaller tumors in Wolbach and Millet's [7] case bring to 4 the cases of tumors arising in locations other than the medullary pia.

Recapitulation.—Certain symptomatic, clinical, laboratory and gross anatomic features of the intradural lipoma are at variance with the corresponding features of tumors of the spinal cord as a whole, and it is possible that attention to these features in the future may make possible the diagnosis of the tumor prior to exposure. Tumors making themselves known before the third year of life, about the beginning of the third decade and about the beginning of the fifth decade of life are suspect. The duration of the symptoms is of little help, but if the history is long lipoma should be especially considered. Pain of various sorts is common in cases of lipoma, but if the pain is definitely radicular, especially if limited to a narrow zone, the presence of lipoma is unlikely, though not impossible. Awkwardness in the use of the hands and ataxia in walking when recited as early symptoms and before weakness was noted suggest lipoma, especially if the patient is young.

Physical findings are of little help. Signs suggesting lipoma are diminution of joint and vibratory sensibility out of proportion to other sensory changes and unilateral flaccid paralysis of an extremity due to an intraspinal tumor. If a lipoma is present, one is not likely to discover a complete manometric block at the time of lumbar puncture, but the fluid will almost certainly contain globulin or excessive protein (frequently

34. Beykirch, A.: Klinischer Beitrag zur Buerteilung der myelographischen Röntgenbilder, Beitr. z. klin. Chir. **142**:301-321, 1928.

only small excesses) or be xanthochromic. Roentgenograms cannot be counted on to reveal bony changes, but if there are evidences of widening of the spinal canal over three, four, five or more vertebrae the presence of a lipoma is suggested. The myelogram cannot be counted on to enable one to diagnose the exact relation of the tumor to the cord. If, in the presence of the suggestive features mentioned, the examination points to a cervicothoracic location for the trouble, the possibility of lipoma is good. The presence of congenital defects, especially a lipoma of the back overlying the suspected segments of the cord, lends confidence to the diagnosis.

Pathologic Features of Intradural Lipomas.—Certain aspects of the pathologic picture of intradural lipoma have been briefly mentioned to point up the discussion of the clinical changes, but a more minute inquiry is now in order. Characteristics which bear looking into are the relation of the fatty mass to the neural tissue and its envelopes, the reactions evoked in the neural tissues and its envelopes, the amount and origin of the stroma and capsule of the tumor, the amount of involvement of roots and the nature of this involvement and the type of fat composing the tumor.

Concerning the exact relation of these tumors to the cord there is little disagreement. After 11 cases are excluded because of lack of sufficient information or because the tumor lay on the roots or the filum terminale, there remain 18 cases which are of importance with respect to the relation to the cord, and in all these cases, with 1 possible exception, the tumor lay on the side of the cord in an extramedullary position but so firmly and intimately attached to the cord that the superficial resemblance was to intramedullary tumor. In every case there was described a layer of connective tissue which separated the adipose tissue from the neural tissue, and in 11 cases (Gowers; Braubach; Ritter; Elsberg [24]; Bielschowsky and Valentin; Fay; Scherer [25]; Guillain, Bertrand and Salles; Bucy and Gustafson; case 2 of this series) the authors stated the opinion that the tumor arose in the pia and that the lamina between the cord and the tumor was of pial origin.

Cases likely to be the subject of controversy over this matter of pial origin and extramedullary location are those of Elsberg,[24] Turner,[23] Jabotinski [22] and Sachs and Fincher.[8] Elsberg described the location of his 2 tumors as "subpial," but that he did not mean by this that they were intramedullary is shown by his classifying them with the extramedullary tumors. Turner's tumor, described as invasive, and probably malignant, presented on the surface, and the fatty portion was separated from the cord by a mass of fibrous tissue which had undergone proliferation.

The tumor described by Jabotinski is the most controversial because the ends of it lay within the medullary substance. A case can be made out for the origin of this tumor within the cord and its secondary migration to a superficial location except for the poles. This mechanism was suggested by Stookey.[21] Contrary to Stookey's statement, however, these tumors show a capsule separating the fat from the cord, but this capsule is not often of such a nature that the tumor can be lifted from it, as in the case of Sachs and Fincher. In Jabotinski's case the presence of roots within the tumor speaks for some origin other than intramedullary, with subsequent migration. To reconcile this tumor with the hypothesis of pial origin it is necessary to suppose that the hyperplastic pial septum invaded the cord at the poles of the tumor and then became filled with fat.

The tumor described by Sachs and Fincher was reported as intramedullary, but attention to the excellent illustrations and the relations described in the operative note leave no doubt that the tumor was separated from the cord by an inner layer of pia and that the only dispute is one of terminology.

Another point of importance is that fat has never been described as lying bare within the neural tissue or with only the sparse stroma that one might reasonably associate with formation of lipoma. Rather, the only fat lying within the cord is associated with the heavy extensions running into the cord from the hyperplastic septum. Jabotinski's case is a possible exception.

The glial and neural elements of the cord respond to the presence of the tumor by degenerating when the pressure or interference with the blood supply becomes critical. In all other instances the cord seems to tolerate the fatty parasite well. The same cannot be said for the connective tissue of the leptomeninges, the pial extensions into the cord or the endoneurium of the roots. Twenty-one cases are pertinent to this phase of the study, in which either necropsy or operation was done and enough tissue was removed to show the nature of the changes.

In 8 of the 21 cases the tumor showed little or no reaction of connective tissue. The tumor in Elsberg's [24] case VI was described as a fibrolipoma, but no mention was made of pial or root hyperplasia and the tumor was removable. Beykirch [34] observed only a fine stroma with few nuclei in his tumor of the cauda equina, but the whole tumor was not removed. The tumor re-

moved by Sachs and Fincher is one of which one may be certain, since it was removed *in toto*, was shelled from the cord and was histologically negative for evidence of hyperplasia of the connective tissue. The tumor described by Bucy and Gustafson had only increased reticulin near its attachment to the cord and a heavy capsule on the free surfaces. Elsberg's description of the tumor in his case VIII was accompanied by photomicrographs demonstrating much more cellularity in one location than in the other, but there was nothing in the description to indicate pial or root hyperplasia. In the cases of Wolbach and Millet [7] and Fay [27] there was minimal "invasion," and though this probably meant invasion by hyperplastic pial extensions, it is safest not to make the assumption. The tumor of the filum described by Spiller [6] is the last of the 8 tumors.

In 13 cases (Gowers [9]; Braubach [28]; Turner [23]; Oppenheim and Borchardt [19]; Ritter [18]; Henneberg [35]; Bielschowsky and Valentin [31]; Scherer [25]; Guillain, Bertrand and Salles [26]; Baker and Adams [30]; Jabotinski [22]; cases 2 and 3 of this series) the extent of changes in the connective tissue ranged from moderate to remarkable. The alterations were by no means similar in all cases. On the one hand are the case of Gowers,[9] in which slight pial thickening and abundant fibrous tissue appeared in the portion of the tumor next the cord, and the case of Bielschowsky and Valentin,[31] in which pial thickening and radicular endoneural proliferation were present; on the other hand are the cases of Scherer [25] and of Guillain, Bertrand and Salles [26] and case 2 of this series, in which there was conspicuous proliferation of the endoneurium of traversing roots. It is probable that in Stookey's [21] case and in cases 1 and 4 of this series the tumors would show a similar picture if they were examined *in toto*. One-half the tumor in Turner's case was fibrous and cellular to such a degree that it was considered sarcomatous. In Ritter's case the tumor contained cellular strands running into the cord and many embryonic fat cells and was considered to be a lipoblastoma.

The question arises whether these proliferative changes were actually induced in the connective tissue by the fat, or whether they constituted the primary defect and the deposition of fat was secondary. This of course is difficult to answer, but it is likely that in some cases merely a pial thickening was secondary to presence of the fat (as would be the adhesion of the dura to the tumor, reported in a few cases), while in other cases both the fat and the proliferation of connective tissue were manifestations of the same process.

The septal and stromal elements of the tumor have connections with the capsule and must be of similar pial origin. A false impression of the amount and nature of the connective tissue present may be obtained if too much attention is paid to the piece of fat removed from the surface of a lesion incapable of being totally removed. Most of the tumors showing pronounced fibrous hyperplasia at the tumor-cord interface are almost wholly fatty in the locations from which one would take a bit for biopsy.

In 15 cases nerve roots traversed the lipoma; in 5 cases they did not, and in 2 cases roots were probably implicated but surgical exploration was not extended to determine this point. In 8 instances (Gowers [9]; Spiller [6]; Ritter [18]; Scherer [25]; Guillain, Bertrand and Salles [26]; Baker and Adams [30]; cases 2 and 3 of this series) the roots were more or less extensively broken up by fat, which in some manner had insinuated itself into the spaces between the individual nerve fibers. Instead of the root fibers traversing the fat in well defined bundles of normal size, the bundles were filled with fat, as though the fat had arisen from an element in intimate contact with the individual fibers or had extensively invaded from without. The appearance of such an area on cross section, especially with the myelin stains, is somewhat like that of the magnetic field of a straight bar magnet when delineated by iron filings on a sheet of paper. Scherer's [25] figure 3 is the most perfect illustration of this iron filing effect imaginable, for it shows the complete pattern. Figure 4 in the article by Guillain, Bertrand and Salles [26] and an illustration in Spiller's report [6] show this effect less completely. Figure 1 *a* of this study represents a small area of a root-bearing field cut on a plane parallel with the fibers, but the field is too small and the magnification too great to demonstrate the iron filing effect.

The fatty tissue of the intradural lipoma is practically never any but adult adipose tissue. In 20 reports the fat was described by this term or by synonymous terms. In an additional 5 cases the tumor was a mixture of adult adipose tissue and fibrous tissue—fibrolipoma. In the case of Ritter [18] all the transitions from embryonic fat to adult fat were shown. Along the capsule and septums this new formation of fat was going on. This lipogenesis, together with the actively growing extensions into the cord and the rapid progression, certainly justifies the desig-

35. Henneberg, R.: Ueber Geschwülste der hinteren Schliessungslinie des Rückenmarks, Berl. klin. Wchnschr. **58**:1289-1293 (Oct. 31) 1921.

nation of liposarcoma. In a single instance (case 2 of this series) tissue suspected of being myxomatous was present.

Granted that the tumor described by Ritter was malignant, were not some of the other tumors malignant, too? Turner's was the only one so described by the author. It is certain that under the influence of either the lipoma or the factor causing the lipoma the fine strands of pia which normally follow vessels into the cord and the septums which extend into the cord from the pia and the root endoneurium become hyperplastic and increase their cellularity. This invasion of pial connective tissue within the neural tube seems to have some of the essential characteristics of malignancy. The tissue appears to be proliferating, though ever so slowly, and the invasion is so pronounced as to make impossible complete local eradication.

The one question on which, it seems to us, the problem of malignancy turns is whether or not these hyperplastic extensions cause destruction of the tissue of the cord. At first glance it seems as though they did, but it must be remembered that no case is pertinent to this discussion if pressure on the cord by the mass of the tumor went unrelieved before destruction of the cord was already present. In cases in which both the invasion and the pressure operate, it is impossible to say which was the cause of the destruction. If one could answer affirmatively the question whether after the almost complete removal of the lipomatous mass the fibrous extensions into the cord continue to grow and to destroy the cord in the absence of recurrence of a pressure-producing mass the process would have to be considered malignant. There is, however, no case in which such an answer can be given. Indeed, certain cases tend to indicate that destruction of the cord does not proceed after removal of the pressure. In the case of Kernohan, Woltman and Adson relief from pressure on the cord was effected by partial removal of the tumor and wide laminectomy, and the condition, instead of continuing to grow worse, became entirely normal and began to regress only after an interval of nine years, when, presumably, the pressure on the cord again became operative.

The validity of this line of thought is greatly diminished because there is no definite evidence that the cord was invaded in the manner under consideration. The cord in case 2 of this series was definitely invaded, and the patient has shown steady improvement over her postoperative condition during the past eight years. Counteracting this result is that in the case reported by Stookey, who secured improvement over a three year period, when regression began. It cannot be said with assurance that any tumor except Ritter's was malignant, and it is our opinion that this cellularity and invasive aspect of the pial extensions into the cord do not constitute malignancy.

Etiologic Aspects of Intradural Lipoma.—The puzzling question of the origin of lipomas in a location ordinarily considered to be devoid of fat cells has received the attention of a number of recent investigators (Ritter [18]; Henneberg [35]; Stookey [21]; Bielschowsky and Valentin [31]; Verga [36]; Krainer [37]; Scherer [38]; Guillain, Bertrand and Salles [26]; Bucy and Gustafson [20]; Jabotinski [22]). As Verga [36] indicated, in speaking of intraspinal and intracranial lipomas as a group, any hypothesis must account not only for the masses of fat within the dura mater but for the constant intimate relation of the tumors to the pia mater, the connective tissue stroma (sometimes osseous in cases of intracerebral lipoma), the frequent association with anomalies of development and the preponderant location in the midline. To these features should be added the predilection for the cervicothoracic junction of the cord and for the dorsal surface of the cord, the frequent early onset and the notable potentiality for growth within the entering posterior roots. It is our opinion that the iron filing effect cannot be explained satisfactorily by invasion of the root from without. No cells visible in these regions appear capable of such an invasion. The fat must be considered to have arisen within the root at the same time as, and as an inseparable feature of, the rest of the fatty mass.

It was shown long ago that, contrary to appearances, the leptomeninges actually do contain small amounts of fat, and Virchow,[39] in 1863, availed himself of this knowledge to explain intradural lipomas, for it was his expressed view that these growths arose from these self same fat cells. As a larger number of cases accumulated, it became apparent that the great majority of lipomas, especially of the brain, occurred in sagittal locations, whereas if any fat cells in the pia were able to proliferate on occasion this distribution should not obtain. Neither does this hypothesis apply satisfactorily to spinal lipomas, none of which have been reported to occur on the anterior sur-

36. Verga, P., cited by Sperling and Alpers.[1]

37. Krainer, L.: Die Hirn- und Rückenmarkslipome, Virchows Arch. f. path. Anat. **295**:107-142 (July 8) 1935.

38. Scherer, E.: (*a*) Ueber die pialen Lipome des Gehirns: Beitrag eines Falles von ausgedehnter meningealer Lipomatose einen Grosshirnhemisphäre bei Mikrogyrie, Ztschr. f. d. ges Neurol. u. Psychiat. **154**: 45-61, 1935; (*b*) footnote 25.

39. Virchow, R., cited by Sperling and Alpers.[1]

face of the cord. The crucial point against Virchow's hypothesis is that adult fat cells do not reproduce themselves (Wells [40]) and that, whatever adult fat cells come from, it is not other adult fat cells.

A second concept was that of Rindfleisch,[41] who described lipomas originating through deposition of fat in newly formed cell aggregates deriving from the connective tissue. He did not associate formation of fat with primitive cells but, rather stated that it is a property of common connective tissue to proliferate and then to become adipose. Unexplained by this hypothesis is the predilection for sagittal locations in the brain and dorsal locations in the cord. Furthermore, fibroblastic cells are probably differentiated cells incapable of giving rise to other types (Maximow and Bloom [42]). Wilson, Bartle and Dean [43] expressed the opinion, however, that the tumor they had described arose through metaplasia of the adult connective tissue of the pia.

A third possibility, briefly mentioned by Gowers, and then dismissed, placed the origin with fatty substances liberated by the degeneration of neural structures.

A fourth hypothesis (Taubner [44]) placed the parentage with glia cells which proliferate and undergo fatty degeneration. Stookey [21] briefly considered a somewhat similar origin from glia which picks up fat abnormally. Weighty evidence lies against any such origin. The capsule of the lipoma and the septums separating the tumor from the cord have been, without exception, of mesodermal, and not of glial, origin. Glia has never been observed to take up fat in a huge uniglobular manner so as to simulate adipose tissue.

The predilection for sagittal locations has been given such importance by some investigators that they have proposed an origin through inclusion of misplaced elements within the closing lips of the neural groove. Bostroem [45] grouped dermoid, epidermoid and lipoma in the same category as inclusion tumors stemming from embryonic error before the 5 somite stage. Della Rovere [46] expressed the opinion that the inclusions causing lipoma were of mesodermal origin. Ernst [47] stated that some portion of the dermal anlage was sequestered in the closing neural tube. Stookey [21] discussed the pros and cons of this hypothesis in considerable detail, and, though he was not entirely satisfied with it, he accepted it as the best of the explanations available at the time.

The very fact that this hypothesis is formulated particularly to explain the sagitally located tumors proves to be its greatest weakness, for while it well explains the tumors in the midline, it is so inflexible that tumors not in the midline must be accounted for on some other basis. How, for instance, may one explain the bilateral lipoma of the medulla lying in the cerebellopontile angle which was observed by Wolbach and Millet or the 2 tumors of Elsberg,[24] which arose from the portion of the cord anterior to the posterior roots, or the many other laterally, or even ventrally, placed lipomas (Misch [48])?

Furthermore, these lipomas are never surrounded by cord tissue, as one would expect if their anlages had been able to get within the closing neural tube. In a single case (Jabotinski's) a portion of the fat was truly intramedullary. These lipomas, lying in the pia as they do, are of, but not in, the cord. This location seems to speak against their having developed from any germ within the neural tube.

In association with spina bifida fatty masses are seen which may arise by the inclusion of fat precursor tissue within the sclerotomes before the neural arch closes, but the absence of extensive spina bifida in the cases in which there are huge intraspinal lipomas speaks against the hypothesis of inclusion as applying to the latter group. Closure of the neural arch is a sensitive process and is liable to interference by minor disturbances, many not even giving rise to clinically detectable lesions, as in the case of spina bifida occulta. That a mass of tissue could become misplaced between the closing neural arches without causing them to stay open seems unlikely. The absence of dural attachments in almost every case is also against such an origin for these tumors. An argument applicable only against the hypothesis of epiblastic inclusion is the constant absence of any ectodermal tissue in the lipomas, except for the infiltrated cord and the nerve roots. The observation that a variety of

40. Wells, H. G.: Adipose Tissue, a Neglected Subject, J. A. M. A. **114**:2177-2283 (June 1) 1940.

41. Rindfleisch, E.: A Manual of Pathological Histology to Serve as an Introduction to the Study of Morbid Anatomy, translated by E. B. Baxter, London, New Sydenham Society, 1872, vol. 1, p. 168.

42. Maximow, A. A., and Bloom, W.: A Textbook of Histology, ed. 2, Philadelphia, W. B. Saunders Company, 1934.

43. Wilson, G.; Bartle, H., Jr., and Dean, J. S.: Intradural Spinal Lipomas, J. Nerv. & Ment. Dis. **91**: 745-753 (June) 1940.

44. Taubner, cited by Sperling and Alpers.[1]

45. Bostroem, E., cited by Sperling and Alpers.[1]

46. della Rovere, D., cited by Ritter [18] and by Stookey.[21]

47. Ernst, P., cited by Sperling and Alpers.[1]

48. Misch, W.: Meningeal Lipomas in the Foramen Magnum, J. Neurol. & Psychopath. **16**:123-129 (Oct.) 1935.

congenital defects are present in cases of intradural lipoma cannot be marshaled as evidence in support of the inclusion hypothesis alone, for it equally supports any hypothesis assuming an origin in defective embryogenesis, whether it is misplacement, abnormal persistence or abnormal differentiation of the anlage.

Another hypothesis of the origin of pial lipomas, advanced by Verga, attributes them to embryonic mesenchyme persisting from the early stages of primitive meningeal formation, which then forms the aberrant lipomatous growths. Krainer reached much the same conclusion, but with embellishments. He concluded that these lipomas were not primarily independent growths; rather, he said that they were malformations of some element in the primitive meninx which, though it differentiated abnormally, continued to behave like the meninx toward vessels and nerves. By this he meant that the fatty masses do not expand and displace nerves and roots, with regard for nothing but their own enlargement. It is as though some part of the primitive meninx, through an unknown defect, oriented its differentiation toward adipose tissue rather than toward fibrous connective tissue. Since the normal pia admits the posterior roots through the pial ring and continues out within the nerve as endoneurium, the adipose pia does likewise. Whatever independent growth the tumor shows is secondary. This hypothesis is attractive, for a number of reasons. It harmonizes with the intrapial location of the tumors and, especially, with the growth within the roots. The shortcomings of the hypothesis are its lack of specificity concerning the exact cells responsible for the formation of the fat, the cause of this formation and its failure to explain the predilection for the cervicothoracic region of the cord.

The possibility of origin in a fat embolus was embodied in a question put to Stookey [21] by Dr. Beverley Tucker during the discussion which followed the presentation of his paper. It has not been considered since.

The most recent proposal is that of Scherer,[38a] who adapted Wassermann's [49] researches on the origin of adipose tissue to pial lipoma. Contrary to the view expressed by Flemming [50] and other investigators that the fat cells are derived from fibroblasts, Wassermann confirmed the hypothesis of Toldt [51] that fat is a specific tissue derived independently of the fibroblasts. In early embryogenesis, when the capillary net is developing in mesenchymal reticulum, the embryonic vessels are surrounded by primitive mesenchymal elements, some of which persist and later give rise to the primitive fat organs which form the nucleus of the fatty lobes and adipose tissue of later life. Adipose tissue is thereby closely related to formation of vessels and is to be considered a part of the reticuloendothelial system. Capillaries are of course everywhere, and the formation of a lipoma becomes easily explicable. This simple hypothesis fails to explain satisfactorily the predilection of lipomas for certain locations, their rarity in a vascular membrane, such as the pia, and the association with other anomalies.

Is it possible to formulate a hypothesis which will explain all the observed facts about these lesions, square with the newer concepts of meningeal origin and fat formation and harmonize, to some extent, the various hypotheses already considered? The following hypothesis seems to do so.

The divergent views of investigators who would derive the meningeal investment entirely from mesoderm (Weed [52]; Flexner [53]) and of others who would assign to the neural crest an important part in the genesis of these structures (Harvey and Burr [54]; Harvey, Burr and Van Campenhout [55]; Raven [56]) seem now to be resolved. The neural tube is early invested by the circumferentially flowing mesenchyme of ectodermal origin—the neural crest. This leptomeningeal anlage is not of single derivation, for mesodermal tissue—endodermal mesenchyme—mingles with it. Before long these two mesenchymes lose their distinguishing characteristics

49. Wassermann, F.: Die Fettorgane des Menschen. Entwicklung, Bau und systematische Stellung des sogenannten Fettgewebes, Ztschr. f. Zellforsch. u. mikr. Anat. **3**:235-328 (Feb.) 1926.

50. Flemming, W., cited by Bell, E. T.: I. On the Occurrence of Fat in the Epithelium, Cartilage and Muscle Fibers of the Ox; II. On the Histogenesis of the Adipose Tissue of the Ox, Am. J. Anat. **9**:401-438, 1909.

51. Toldt, C., cited by Bell, E. T.: I. On the Occurrence of Fat in the Epithelium, Cartilage and Muscle Fibers of the Ox; II. On the Histogenesis of the Adipose Tissue of the Ox, Am. J. Anat. **9**:401-438, 1909.

52. Weed, L. H.: The Development of the Cerebro-Spinal Spaces in Pig and in Man, Washington, D. C., Carnegie Institution of Washington, 1917.

53. Flexner, L. B.: The Development of the Meninges in Amphibia: A Study of Normal and Experimental Animals, Washington, D. C., Carnegie Institution of Washington, 1929.

54. Harvey, S. C., and Burr, H. S.: The Development of the Meninges, Arch. Neurol. & Psychiat. **15**: 545-565 (April) 1926.

55. Harvey, S. C.; Burr, H. S., and Van Campenhout, E.: Development of the Meninges: Further Experiments, Arch. Neurol. & Psychiat. **29**:683-690 (April) 1933.

56. Raven, C. P.: Zur Entwicklung der Ganglienleiste: V. Ueber die Differenzierung des Rumpfganglienleisten-materials, Arch. f. Entwcklngsmechn. d. Organ. **134**:122-146 (March 9) 1936.

and become more differentiated in their progress toward the adult pia-arachnoid. Further differentiation is dependent on the extramedullary passage of ventricular fluid. The surrounding mesoderm forms the dural lamina, but even this is not pure endodermal mesenchyme, for neural crest elements contribute to it.

Whether the vascularization of this compound pial anlage is accompanied by invasion of vessels from without or by formation of capillaries within its substance is of no importance to this discussion. The point is that both the pial anlage and the surrounding mesenchyme are of compound origin and become a more differentiated tissue composed of an apparently single element before vessels appear in the pia. Any fat appearing in the meninges must come from mesenchymal cells persisting around the capillaries. These mesenchymal cells are somehow prevented from forming fat in all but a few cases, and it may be hypothesized that this potentiality is almost completely held in abeyance by some local peculiarity of the tissue resided in. Perhaps the presence of mesenchyme of ectodermal origin exerts this influence. Formation of fat in other organs and locations is held in check for reasons which must be resident in the specific locations. The check on formation of fat fails because of some deficiency of the crest elements in the developing pia in certain locations. That this deficiency is but a part of a more or less generalized defect of ectoderm is suggested by the occurrence of other congenital defects, almost all of which originate in ectodermal faults.

Reasoning from the predominance of subcutaneous lipomas over the upper part of the back, the shoulders and the neck and the location in these segments of the interscapular gland of some animals (Geschickter [17]), one may say that the potentiality for formation of adipose tissue in these segments is greater and the orientation toward formation of fat in the pia of these segments is stronger than in other locations because of its derivation from similar mesenchyme, and consequently it more often overcomes the checking influence. The predominantly dorsal location on the cord and the failure of the fat to encircle the cord completely may be due to the fanning out of the crest elements as they flow around the cord, so that as more anterior positions are reached the deficient region is adequately covered by nondefective crest from adjacent segments. This hypothesis explains the intimate association of fat in roots because the roots penetrate a pia destined to become adipose and the fat actually develops in the pial ring and endoneurium. The hyperplastic nature of the strands invading the cord from the inner surface of the septum separating the cord from the tumor is perhaps to be regarded as a preparation for transformation into adipose tissue. Formation of fat in these strands is an observed fact.

Whether this panniculus adiposus of the pia is to be regarded as a neoplasm or as a malformation, as Krainer would have it, is a difficult question. The tumor described by Braubach did not respect the nerve roots, for it displaced them anteriorly and, though these root fibers were said not to be severely degenerated, the arm served by them was paralytic. Certain tumors (Ritter; Oppenheim and Borchardt; Stookey; Bucy and Gustafson) had free poles, a feature indicating that the fatty mass increased in a longitudinal direction so that it spilled over the ends of the region giving rise to it. This may or may not indicate independent growth. If we may disregard for the moment the question of independent growth, it appears to us that there is no essential difference between the formation of fat in greatly abnormal amounts in the pia and the formation of an abnormal mass of fat in the subcutaneous tissue. Both processes require the proliferation of fat precursor cells and subsequent differentiation into the adult type. Both processes imply a failure of regulatory activity. From a philosophic point of view both masses are to be regarded as neoplasms.

EXTRADURAL LIPOMA

The cases of fatty tumors lying outside the dura are neither so numerous nor so adequately reported as cases of the intradural variety. A large percentage were reported during the previous century, and there has been no increase in the number of cases recorded recently, such as was observed with the tumors inside the dura. This perhaps is to be explained by the fact that there has been a recent renewal of interest in the formation and nature of the leptomeninges and fatty tumors in this location are regarded as of special significance. Extradural lipoma, however, is of a commoner cut, needing no special explanation, exciting less interest and more often going unreported.

Table 2 lists the cases of extradural lipoma in chronologic order. Additional data on 3 cases of extradural lipoma observed at the Mayo Clinic (cases 18, 19 and 20 of table 2) follow.

CASE 5.—A man aged 49, a merchant, registered at the clinic on May 6, 1912, with the complaints of weakness of the legs associated with spasms which doubled up the legs, pain in the back which extended around the body and difficulty in starting the flow of urine.

The family history and the patient's previous medical history were noncontributory. The trouble had begun

TABLE 2.—*Data on Twenty Cases of Extradural Lipomas*

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	Year	Author	Sex	Age of Onset, Yr.	Duration	Level	Spinal Puncture	Roentgenographic Changes	Other Disorders	Pathologic Change	Outcome
1	1834	Robarts [57]	F	24	5 yr.	T10 to T12				Fatty tumor	Necropsy
2	1847	Chapelle: Bull. Soc. anat. de Paris **22**: 6-7 (Jan.-Feb.) 1847	F	2½	1½ yr.	Entire spinal cord; greatest at conus			Obesity	Adult fat	Necropsy
3	1847	Albers, J. F. H., cited by Stookey [21]	..	..	.....					Lipoma	Necropsy
4	1852	Obré: Tr. Path. Soc. London **3**: 248-249 (April 6) 1852	..	1?	2 yr.	Upper thoracic; T1 and T2 (?)				Adult fat	Necropsy
5	1857	Virchow, R.: Virchows Arch. f. path. Anat. **11**: 281-288 (March) 1857	M	53	3 mo.	Upper lumbar; L1 and L2 (?)			Multiple similar tumors	Myxomatous lipoma	Necropsy
6	1869	Hoffmann, cited by Stookey [21]	F	42	9 mo.	Multiple tumors from T7 to sacrum			Other lipomas in dorsal roots; glioma of cord	Adult fat (?)	Necropsy
7	1890	Berenbruch [60]	M	16	2½ mo.	Thoracic (?)			Lipomas of back; angiolipoma of renal capsule; angioma of cord	Angioma with fat cells	Operation; necropsy
8	1895	Starr, M. A.: Am. J. M. Sc. **109**: 613-637 (June) 1895	F	50	4 mo.	T10 and T11; two tumors				Adult fat	Operation; death
9	1897	Strümpell, in discussion on Arch. f. Psychiat. **29**: 1004, 1897	..	..	.....					Adult fat	.....
10	1901	Liebscher, C., cited by Stookey [21]	F	51	4½ yr.	T7 to T8				Angiolipoma	.....
11	1918	Frazier [10] *	F	55?	.....					Angiolipoma	.....
12	1925	Sachs [59] †	M	13	1 yr.	T6 to T7 (?)			Gibbus at level of tumor	Adult fat without capsule	Operation; recovery
13	1925	Pick [58]	F	Young adult	.....				Gibbus at level of tumor	Adult fat (?)	.....
14	1928	Elsberg, C. A.: Surg., Gynec. & Obst. **46**: 1-20 (Jan.) 1928	..	33	3 mo.	T8 to T9 (?)			Multiple lipomas	Embryonic fat	Operation; recovery
15	1929	Kasper and Cowan [61]	M	6	.....	C2 to T8 and L3 to sacrum; 2 tumors	No block; globulin present			Vascular lipoma	Necropsy; death from lumbar puncture
16	1931	Petit-Dutaillis and Christophe: Rev. neurol. **2**: 824-827 (Dec.) 1931	F	43	1 yr.	T6 to T10	Complete block; 800 mg. of protein per 100 cc.	Bone normal; partial obstruction to iodized poppyseed oil		Angiolipoma	Operation; recovery
17	1939	Ingebrigtsen and Leegaard: Acta chir. Scandinav. **82**: 271-281, 1939	M	22	7 mo.	T7 to T9				Myxolipoma	Operation; recovery
18	1944	Case 5, this series	M	48	1 yr.	T9		Spinal column normal	Obesity	Adult fat (?)	Operation; improvement
19	1944	Case 6, this series	F	30	3 yr.	T6 to T8	Partial block; 30 mg. of protein per 100 cc.	Spinal column normal	Obesity	Angiolipoma	Operation; recovery
20	1944	Case 7, this series	M	67	1 yr.	T8 to T9	Partial block; 75 mg. of protein per 100 cc.	Spinal column normal		Angiolipoma	Operation; recovery

* This report tabulated 2 angiolipomas. One may have been Liebscher's, but the other was not previously reported; we here include it with the information available.
† Sachs did not consider this a lipoma, but it continued to increase in size after it had fulfilled the function ascribed to it. It compressed the cord, and we consider it lipomatous for our purposes.

one year prior to registration in the clinic, when the right leg became weak for three weeks and then returned to normal. Six months before registration the left leg began to weaken and in three months became so weak that the assistance of a cane was required in walking. A month later the right leg again became weak, and the patient was soon unable to stand. Then there developed flexor spasms in the leg and a pain in the back, which extended about the body. No mention was made of exaggeration of this pain at night or on straining. Soon all voluntary motion had departed from the legs. Constipation and the urinary difficulty completed the picture. The weight had dropped from 220 to 165 pounds (100 to 84 Kg.) in an unstated period.

Examination revealed a painful zone over the midthoracic spinous processes, a sensory level at the ninth thoracic dermatome below which touch was normal but appreciation of heat and cold was absent, severe spastic paraplegia, increased patellar and achilles reflexes, ankle clonus and a Babinski sign bilaterally. Roentgenograms of the spinal column revealed nothing abnormal.

On May 16, 1912 laminectomy of the fifth to the eighth thoracic vertebrae was performed. Just as the lower part of the incision was being dealt with in a location where the intraspinal contents seemed enlarged, the patient's condition became alarming and the incision was closed. Eight days later additional neural arches, extending from the lower end of the previous incision, were removed, together with an extradural lipoma.

The surgeon was inclined to be hesitant in ascribing the trouble to this fatty mass, but four years later the patient reported that he had had steady improvement and was walking with a cane. Laxatives were required, but he had good vesical and rectal control. Slight numbness was present in the legs. The spasms had disappeared. The eventual outcome is unknown.

The specimen is no longer available, and no description of the tumor was given except that it was called a lipoma.

Case 6.—A white woman aged 33, a housewife, registered at the clinic on Aug. 2, 1933, with the complaint of weakness of the legs, urinary urgency and numbness extending to the waist.

The family history was of possible significance. Obesity was a trait of the patient's maternal ancestors. One sister was obese, and her mother died of diabetes and paralysis. The patient weighed only 98 pounds (44 Kg.) when she married, but with each of four pregnancies she gained 20 to 30 pounds (9 to 14 Kg.), and at the time of registration she weighed 202 pounds (92 Kg.), although she was short.

The patient's trouble had had its onset on Dec. 28, 1930, at which time she was in the third trimester of pregnancy. While she was attending her mother's funeral her feet became numb. This numbness slowly increased but did not occasion any alarm until Feb. 4, 1931, when, during parturition, she suddenly lost all sensation and motion from the upper part of the abdomen down. A week and a half later there was no improvement, and the patient was told that she could never recover. The next day she could wiggle her toes. By May 1931 her condition had improved to such an extent that her feet merely felt heavy and slightly numb, and she was able to do all her own work. This status obtained until December 1932, when she suddenly became numb to the waist. Increasing paraparesis and urinary urgency began soon afterward.

The results of physical examination were unremarkable except for the obesity and the neurologic signs. There was complete anesthesia from the costal margin down except for an area of seemingly normal sensitivity in the right lower sacral and coccygeal dermatomes and areas of only moderately diminished sensitivity over the lower portion of each calf and the posterolateral aspect of the left hip and thigh. Joint and vibratory sensibilities were absent as high as the iliac spines. Power in the legs was moderately diminished, without any particular muscle groups being selectively affected. The abdominal reflexes were absent. A Babinski sign was obtained bilaterally. The patellar and achilles reflexes were moderately hyperactive but equal on the two sides. There was no clonus. The heel to knee and the Romberg test gave results indicative of disturbance of the proprioceptive sense. The tone of the anal sphincter was normal.

Roentgenograms of the spinal column and thorax revealed nothing abnormal, and results of routine examination of the blood, urinalysis and flocculation tests were normal. Lumbar puncture revealed an initial pressure of 12 cm. of fluid, and the pressure rose to 36 cm. after ten seconds of jugular compression. Ten seconds after release of the compression the pressure was 30 cm.; after an additional ten seconds it was 28 cm., and it then fell to 7 cm. The protein amounted to 30 mg. per hundred cubic centimeters of cerebrospinal fluid.

On Aug. 8, 1933, 4 cc. of iodized poppyseed oil was injected into the lumbar subarachnoid space, and a complete obstruction was demonstrated at the level of the eighth thoracic vertebra. The following day laminectomy of the eighth to the sixth thoracic vertebrae was performed, and a reddish yellow mass, 10 cm. long, 2.5 cm. wide and 1.5 cm. deep, was observed on the posterior surface of the dura. The dura was very thin under the mass, and the cord seemed to be flattened to about two-thirds the normal thickness. The tumor and the surrounding bone were vascular. Total removal of the tumor was effected.

Twenty days after the operation the patient estimated her motor improvement at 25 per cent and her sensory return at 75 per cent. Examination demonstrated that appreciation of light touch had returned to normal in all areas, while pain and temperature sensibilities had improved greatly. Joint sense was normal, but vibratory sense was greatly reduced over the right ankle. The tendon reflexes were the same as before. The abdominal reflexes were barely elicited, and the Babinski sign could no longer be obtained on the right side. Examination a year later revealed that her neurologic condition was normal. A letter from her, dated Sept. 8, 1943, stated that she had been doing all her own work since the operation and that she was free of symptoms except for mild lameness in the back and occasional sick headaches.

The tumor was of soft consistency, and its surface was traversed by delicate fibrous strands. The gross and microscopic features were the same in all parts of the tumor. The sections showed that the tumor was composed of a mixture of fatty and vascular elements (fig. 7*a*). It is estimated that the fatty tissue constituted two thirds and the vascular tissue one third of the tumor. The vessels were mostly the size of small veins, and their walls were invariably thin, being composed of slender collagenous bands, bearing a few fibrocytic cells oriented with the circumference of the vessels. The attenuated walls of the fat cells lying between the vessels made dichotomous junctions with the walls of the vessels. In a number of locations, especially where the vessels lay close to one another

and were not separated by fat, the vessels were observed to be connected by light collagenous tissue bearing cells with lightly stained cytoplasm and oval to elongate vesicular nuclei. A few small arteries and arterioles were evident in the tumor, and a few fibrous septums partitioned the tumor in an incomplete fashion. These septums were unremarkable histologically and were unobtrusive. The fat cells which filled the spaces between the vessels were all of adult adipose tissue type and no embryonic, xanthomatous or myxomatous regions or cells were present.

CASE 7.—A man aged 68, a railway coach carpenter, registered at the clinic on Oct. 5, 1942, complaining of burning sensations and progressive weakness and incoordination of the legs and swelling of the feet toward the end of the day.

The family history and the patient's previous medical history were unimportant. The swelling of the feet had begun in September 1941; it had not been bothersome, had affected the right foot more than the left and had not been associated with other symptoms until April 1942, when the burning sensation appeared in the right foot. In a few weeks the left foot began to burn similarly, and in a few more weeks the burning ascended both legs to the groins. This sensation was more severe on the anterior than on the posterior aspects of the legs. The soles of the feet felt as though he were walking barefooted on cinders. In June 1942 weakness and lack of coordination of the legs made their appearance and steadily increased in severity. The right leg had given more trouble than the left. Examination did not reveal signs of significance except in the nervous system. Cutaneous sensibilities were moderately diminished over both legs. Vibratory anesthesia was complete to the iliac crests, while joint sense was greatly diminished in the toes of the right foot and less so in the toes of the left foot. The gait was of spastic type, and ataxia was prominent. The right leg was demonstrably weakened and spastic, but not so the left leg. The patellar reflexes were increased but equal on the two sides. The achilles reflexes were unequal on the two sides, the response on the right side being the stronger. The Babinski sign was present bilaterally, being stronger on the right side than on the left.

Roentgenograms of the spinal column revealed nothing significant. On lumbar puncture the rapid rise but slow fall of the fluid suggested a partial block. The spinal fluid was colorless; the serologic reactions were negative, and the total protein amounted to 75 mg. per hundred cubic centimeters of fluid. After the lumbar puncture vague impairment of sensation appeared below the twelfth thoracic dermatome. Iodized poppyseed oil injected into the caudal subarachnoid space demonstrated a protruded disk at the first lumbar interspace on the left side and complete obstruction to the upward passage of the oil at the level of the eighth thoracic vertebra, apparently due to a mass lying dorsal to the cord.

On October 16 laminectomy of the eighth and ninth thoracic vertebrae was performed with local infiltration anesthesia, and a soft, reddish yellow, extradural tumor, measuring 2 by 3 cm., was exposed. This was easily separated from the dura, and the incision was closed after immediate examination of frozen tissue had revealed a vascular lipoma.

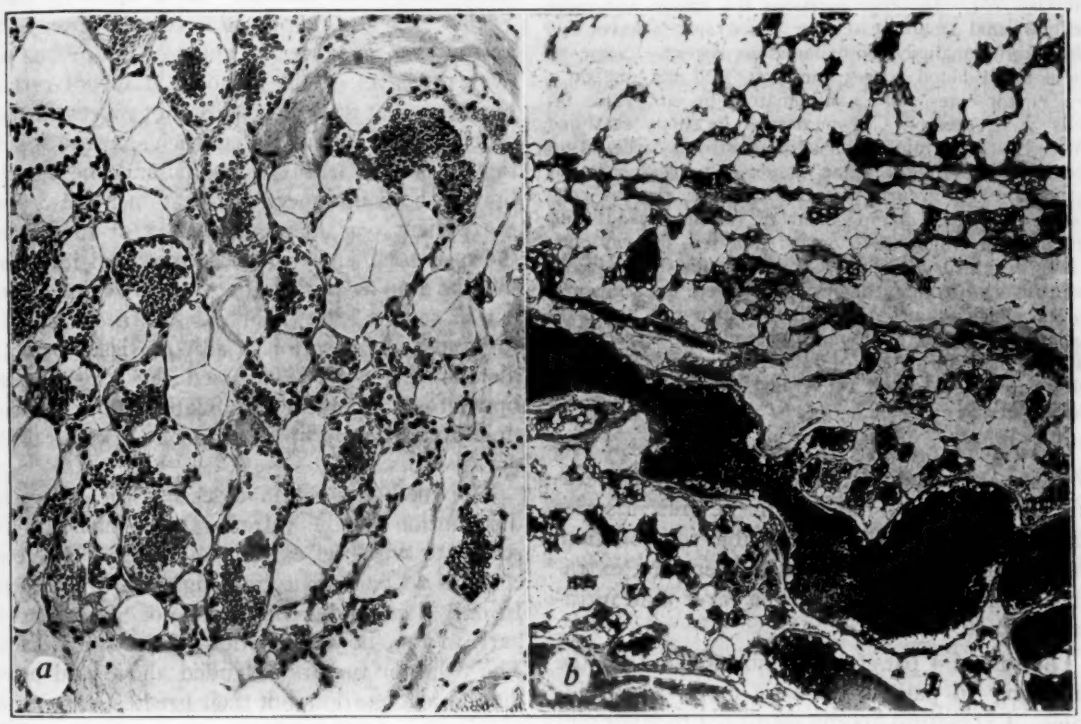

Fig. 7.—(*a*) Extradural lipoma (case 6), showing small, thin-walled cavernous blood spaces interspersed with adipose tissue of adult type (hematoxylin and eosin stain; × 150). (*b*) Extradural lipoma (case 7), showing its angiomatous and lipomatous nature. The vessel walls are slightly thicker; the variation in the size of the vessels is greater, and there is more connective tissue present than with the tumor shown in *a* (hematoxylin and eosin; × 45).

Neurologic examination on October 29 showed only diminution of appreciation of touch, pain and temperature on the lateral aspects of both thighs, moderate diminution of vibratory and joint senses in the legs and a weak Babinski sign bilaterally. Strength in both legs was normal; the tendon reflexes were equal on the two sides, but the patellar reflexes seemed somewhat hyperactive. A recent letter indicated that recovery has been complete.

The surgical specimen was without external markings of note. The histologic appearance of this tumor closely approximated that of the tumor in case 6 except that the vessels displayed more variation of size and the tumor was distinctly more cellular in places. There were areas where the mixture of fat and vessels corresponded to the appearance of the tumor in case 6. In other regions the character of the tumor approximated that of a cavernous hemangioma, with large dilated, tortuous blood spaces separated by but little fat (fig. 7*b*). In other locations the tumor was more cellular, and small vessels or blood spaces gave it a distinctly hemangioendotheliomatous aspect. Some of these small blood spaces accommodated but one or a few erythrocytes. No xanthomatous or embryonic fat cells were present. In numerous locations scattered throughout the tumor the adipose stroma widened to become a patch of cellular tissue, seeming capable of activity. The ground material in these regions consisted of a loose arrangement of fibrous strands and reticulin, in which there appeared a few lacunas containing erythrocytes. The cells of this tissue were fusiform and contained oval, elongated or crescentic nuclei, which stained more lightly than the fibrocytic nuclei. There were no mitoses, and one searched in vain for new formation of fat. All the fat-containing cells were typical adult cells filled with a single large globule of fat.

Clinical Features of Extradural Lipoma.—The 17 cases of extradural tumor found in the literature and the 3 cases reported in the present series make a total of 20 cases available for collation. On the basis of reported cases, therefore, extradural lipoma appears to be even rarer than intradural lipoma.

The sex of 4 patients was not stated. Of the remaining 16 patients, 7 were males and 9 females. Extradural lipoma seems not to favor any age, for it occurs with about equal incidence throughout the life span. The youngest patient was 1 year old and the oldest almost 70 (fig. 3). The duration of symptoms was rather short (fig. 4). Robarts'[57] patient had had symptoms for five years, and this was the longest duration in the entire series. Many of the patients had had trouble for but a few months. Only 4 had a history extending back two years or more. The median duration was about one year.

The outstanding complaint was one of weakness of the legs. Girdle pains were prominent in the recital of symptoms in 3 cases. The results of physical examination were unremarkable on the whole. In 1 case (case 5 of the present series) a peculiar dissociation of sensation was exhibited; the temperature sense was absent below the ninth thoracic dermatome, but the sense of touch was everywhere normal. Spinal puncture was performed in 4 cases. In 3 of these cases examination revealed a manometric block. In the 1 instance in which the manometric reading was normal the fluid contained globulin. In 2 of the 3 cases in which fluid was obtained in the presence of obstruction the protein content was increased; in the other case the protein was normal.

In few of the cases of extradural lipoma were there congenital defects. In 2 cases (Pick[58]; Sachs[59]) severe kyphosis developed after birth, and in each instance the angle of the gibbus was over the level of the tumor. It is not certain, however, that these 2 cases do not represent some other condition. In Berenbruch's[60] case the patient was born with one lipoma and one vascular lipoma, both in superficial locations. In 3 cases the patient was obese, and in 1 of these cases there was a history of obese maternal forebears. We have no assurance that obesity was not present in some of the other cases. In 3 cases disturbances of formation of adipose tissue or of fat metabolism were evidenced by "generalized lipomatosis" (multiple lipomatosis[?]), by multiple myxomatous lipomas and by lipomas of the dorsal roots.

The method used in assessing the segmental distribution of the intradural lipomas was resorted to with the extradural variety. The conclusions to be drawn from figure 8 are evident. In only 2 cases did the tumor not lie, at least in part, in the thoracic portion of the spinal canal. The 3 larger tumors extended above and below the thoracic portion, but their greatest extent was within this portion of the canal. The sixth to the ninth thoracic segments were the areas most often affected. Nearly all the extradural lipomas developed on the dorsal aspect of the dura.

In gross and histologic features extradural lipoma is unlike intradural lipoma. Half of the 20 tumors were definitely or presumably of ordinary adipose tissue. Many of these tumors were described long ago, without histologic study. The remaining 10 tumors were of three types: Seven were mixtures of adult fat and vessels of various sizes and quantities. One of these (Beren-

57. Robarts, H. P.: Case of Disease of the Spinal Cord with Observations, London M. Gaz. **13**:946-950 (March 22) 1834.

58. Pick, L., cited by Sachs.[59]

59. Sachs, E.: An Unusual Case of Paraplegia Associated with Marked Gibbus and a Localized Collection of Fat at the Site of the Gibbus, J. Bone & Joint Surg. **7**:709-719 (July) 1925.

60. Berenbruch, K., cited by Stookey.[21]

bruch[60]) was an angioma with fat dispersed through it. Another (Kasper and Cowan[61]) was described as a lipoma with moderately large, blood-filled vessels. Five tumors were mixtures of angioma and lipoma in such proportions as to be best characterized as angiolipomas. Figure 7 shows the justice of this designation. Two tumors were mixtures of adipose tissue and myxomatous material. One tumor was said to be of embryonic fat, but no further description was given. As mentioned before, the photomicrograph presented with this case suggests that myxomatous material was also present.

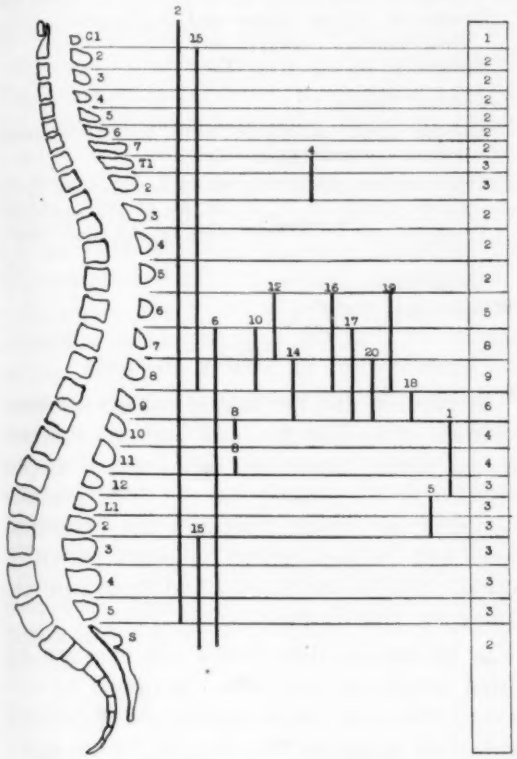

Fig. 8.—Longitudinal distribution of the extradural lipomas with reference to the spinal column. The numbers at the top of the tumors refer to the cases as enumerated in table 2. The column at the right indicates the total number of times each segment is involved by tumor. The tumor numbered 16 extended two segments farther down than is indicated.

Etiologic Factors of Extradural Lipoma.—Little is to be found in the literature concerning the genesis of lipoma from the extradural fat. Robarts speculated that the tumor reported by him arose in the blood clot supposed to have been produced by the blow to the back sustained two years prior to the onset of symptoms. The remarkable feature of the extradural lipoma is not that it occurs but that it does not occur more often. Though the extradural fat is considered to be less fibrous and more buttery than the subcutaneous fat, there is nothing essentially different about it which would explain the paucity of lipomas originating from it.

The extradural fat is more vascular than the subcutaneous fat, owing to the presence of the meningorachidian veins lying in association with it. The persistence of these vessels into adult life suggests that this tissue was much more vascular in embryonic life before the differentiation of the vascular plexus into the adult form. The researches of Wassermann and others indicating the common origin of the endothelium and the fat organ and the potentiality of the mesenchymal cells about the capillaries of adult life for the development of either vessels or fat have been mentioned. That 7 of 20 extradural lipomas were angiomatous cannot but have significance. It is probable that the lipoma of which we speak originates from certain of these bipotential cells. The disposition of these cells to form vessels is well demonstrated by the angiomatous character of the lipoma, and this angiolipoma points to the common parentage of the pure lipoma and the pure angioma—tumors so different in appearance, yet pathologic brothers.

Three facts must be taken into consideration in any speculations on the etiologic factors concerned with extradural lipoma. First, the tumor does not seem to be of congenital origin because it occurs at all ages and the duration of symptoms is short; it is unlikely therefore that the tumor is present for a long time before giving evidence. Second, the segmental distribution is not that of the intradural lipoma or of subcutaneous lipoma; rather, it is that of the meningioma. Third, in an inordinate number of cases this tumor is associated with obesity and multiple lipoma.

Is this tumor actually a meningioma? A tumor which is a meningioma beyond dispute because of the presence in it of masses of cells of the arachnoid cap type as the principal component may, of course, contain fat. The fat may occur scattered about the tumor and in some regions may be rather heavily deposited, but there is no difficulty in finding other regions in which sheets of plump cells, whorls or psammoma bodies are displayed. Photomicrographs of small regions of lipoblastic meningiomas presented with descriptions of these tumors are likely to be misleading because of the pardonable zeal of the authors to show the fatty parts more effectively.

In no case of the extradural lipoma, on the other hand, did the tumor contain regions of cells

61. Kasper, J. A., and Cowan, A.: Extradural Lipoma of the Spinal Canal, Arch. Path. **8**:800-802 (Nov.) 1929.

anything like arachnoid cap cells. In case 7 of this series the tumor contained small islands of scattered cells, but they did not appear to warrant one's calling the tumor meningiomatous. The preponderance of the growths in the thoracic region of the spinal column suggests the possibility that the tumor is a meningioma. This is countered by the fact that all the tumors lay on the external surface of the dura, without any penetration of this membrane. No lipomatous tumor has been observed attached to the inner surface of the dura except the 2 pial lipomas, which had secondary attachments and tumors of the type which is indubitably meningioma (Brown [62]), as mentioned previously. A further argument against this lipoma's being a meningioma lies in the absence of recurrence after simple cleavage from the dura without removal of the attachment. The subject of case 6 of this series was well more than ten years after such a removal. Whatever may be the cause of the lipomatous and angiomatous development from the fat, it is probably not any influence of the arachnoid or its derivatives. The occurrence of obesity and multiple lipoma indicates that the cause is to be sought in some abnormality of the fat organ.

CLASSIFICATION

Cornil and Mosinger [63] proposed a classification of six types of intraspinal lipomas based on the relation of the tumors to the intraspinal content: (1) intramedullary lipoma, (2) intradural extramedullary lipoma, (3) extradural lipoma, (4) radicular lipoma, (5) lipoma of the filum terminale and cauda equina and (6) multiple lipoma. At the time of the report by these authors no instance of lipoma of the roots, other than of the cauda equina, was known, and their fourth group was therefore theoretic. Case 3 of this series is an instance of a lipoma of a root in the thoracic region and so brings the fourth group of Cornil and Mosinger into the realm of the actual. Except for clinical purposes, there seems to be no reason for separation of lipomas of the cauda from lipomas of other roots. The tumors are so rare that even on this basis the separation appears undesirable. The intramedullary group become theoretic if the tumor reported by Schmieden and Peiper [11] is considered other than a lipoma, as has been suggested.

The 49 cases of intraspinal lipoma considered in this paper are capable of rational classification on a combined anatomic and pathologic basis. In this proposed classification each type is more homogeneous than those of Cornil and Mosinger, and certain groups carry implications of clinical and surgical importance. The numbers in parenthesis following the individual types refer to the cases as numbered in tables 1 and 2.

Extradural lipoma
- Tumor of adult adipose tissue (cases 1, 2, 3, 4, 6, 8, 9, 12, 13 and 18)
- Tumor of adult adipose tissue and blood vessels (angiolipoma) (cases 7, 10, 11, 15, 16, 19 and 20)
- Tumor of adipose tissue and myxomatous tissue (myxolipoma) (cases 5 and 17)
- Embryonic lipoma (case 14)

Intradural lipoma
- Massive tumor associated with severe congenital defects (cases 7, 14 and 25)
- Circumscribed pial tumor (cases 2, 3, 5, 6, 8, 10, 11, 12, 13, 16, 18, 19, 20, 21, 22, 23, 24, 26, 27 and 29)
- Tumor of the intradural roots or the filum terminale (cases 4, 17 and 28)
- Liposarcoma (case 9)
- Myolipoma (case 1)

RELATION TO OTHER DISEASES

The relation that the intraspinal lipoma bears to certain other diseases is of interest, and perhaps of some importance with regard to the causation of the related tumor. The probable absence of any relation between the extradural lipoma and the meningioma has already been indicated. Similar conclusions may be drawn concerning the pial lipoma.

The probability that lipoma and angioma are related neoplasms has been mentioned in connection with the causal factors in extradural lipoma. It is strange that the pial lipoma is not sometimes angiomatous, since it arises in a vascular membrane which sometimes gives rise to angiomatous masses. This brings to mind the case reported by Cobb,[64] in which a hemangioma of the medullary pial sheath was accompanied by vascular nevuses of the skin in the dermatome served by the affected segment of the cord. There arises the question of the relation between this occurrence and the instances of pial lipoma accompanied by lipoma overlying the lesion of the cord. These cases seem to indicate the participation of common mesenchyme with an abnormal potentiality for formation of tumor in the genesis of the pia.

62. Brown, M. H.: Intraspinal Meningiomas: A Clinical and Pathologic Study, Arch. Neurol. & Psychiat. **47**:271-292 (Feb.) 1942.

63. Cornil, L., and Mosinger, M.: Des lipomes intrarachidiens, Arch. de med. gén. et colon., 1933, p. 220; book review, Rev. neurol. **1**:634 (April) 1934.

64. Cobb, S.: Hemangioma of the Spinal Cord Associated with Skin Naevi of the Same Metamere, Ann. Surg. **62**:641-649 (Dec.) 1915.

Adair, Pack and Farrior[65] drew certain parallels between multiple lipomatosis and the multiple neurofibromatosis of Recklinghausen. They pointed out that the tumors in certain cases of multiple tumors of nerves are not all of one type, some being neurofibromas and some lipomas. On the basis of these cases of mixed tumors and the many similarities between neurofibromatosis and multiple lipomatosis brought out in the present study, it appears that intraspinal lipoma is in this category. Intradural (pial) lipoma originates in part from the endoneurium of nerve roots, which is of the same material as the pia. In rare cases an intradural lipoma arises solely from roots. Extradural lipoma may be accompanied by multiple lipoma. The question is certainly not simplified by the fact that the lipoma actually noted to involve roots by reason of its origin from the endoneurium (pial lipoma) is not accompanied by multiple lipoma in the sense of Adair, Pack and Farrior while the tumor not springing from roots (extradural lipoma) may be so accompanied.

Whatever the relation between lipoma and neurofibroma may be, it is obscure. Neurofibromatosis has been related to tuberous sclerosis, Lindau's disease and Sturge-Weber disease, and the group of diseases has been termed congenital ectodermoses (Yakovlev and Guthrie[66]) and phacomatoses (Brouwer, van der Hoeve and Mahoney[67]). There appear to be reasons for including multiple lipomatosis in the group as a fifth type. The intraspinal lipoma may, therefore, bear some relation to the aforementioned diseases, but that is a subject for future consideration.

SUMMARY AND CONCLUSIONS

Nearly 1 per cent of intraspinal tumors are lipomas. Three fifths of the lipomas are intradural, and two fifths are extradural.

The distribution between the sexes is about equal for the two varieties of intraspinal lipoma.

The onset of symptoms of intradural lipoma, with few exceptions, is before the age of 2 or 3 years, at the beginning of the third decade or at the beginning of the fifth decade. Symptoms of extradural lipoma appear at any age.

The duration of symptoms of intradural lipoma (before death or surgical removal) ranges from a few months to more than fifteen years. The median duration is about four years. The duration of symptoms of extradural lipoma is usually short, the median being about one year.

The clinical expression of intradural lipoma is distinctive for five reasons: (*a*) Definite root pains are uncommon despite the frequent involvement of roots by the tumor; (*b*) ataxia of the extremities due to deficit of position sense is occasionally one of the first manifestations of the lipoma; (*c*) unilateral flaccid paralysis of an arm associated with spastic paralysis of the legs is sometimes observed; (*d*) complete subarachnoid block is unusual despite the large size to which the tumor grows; (*e*) discoverable changes in the spinal roentgenogram may be absent, but, on the other hand, the spinal canal may be widened for a considerable distance.

Intradural lipoma occurs most commonly in the cervicothoracic region of the spinal cord. Extradural lipoma is most common in the lower part of the thoracic region. Both types of lipoma are far more common on the dorsal surface of the structure giving rise to them than on other surfaces.

All but 1 of the intradural lipomas were composed of adult adipose tissue or of adult adipose tissue with excessive fibrous stroma. Only half of the extradural lipomas were of adult adipose tissue; most of the remainder were angiomatous; a few were myxomatous; 1 was of embryonic fat.

Roots traversed the intradural lipoma in most cases, and it was common to see the fat lying in such intimate relation to the finer structures of the root as to lead to the supposition that the fat developed within the root and did not secondarily infiltrate it.

Intradural lipoma is invariably observed to be separated from the neural tissue by a layer of fibrous tissue of pial derivation. A pial sheath covers the free surfaces of the tumor. Therefore the intradural lipoma is of pial origin.

The connective tissues associated with pial lipoma show certain changes of a proliferative nature: (*a*) The endoneurium of traversing roots proliferates to form prominent fibrocellular masses within the lipoma; (*b*) the pial septum between the tumor and the cord thickens and sends heavy extensions into the cord; (*c*) the pial capsule over the surface of the tumor thickens and may become adherent to the arachnoid and dura.

The apparent invasiveness of the connective tissue with regard to the cord is probably not an expression of malignancy.

65. Adair, F. E.; Pack, G. T., and Farrior, J. H.: Lipomas, Am. J. Cancer **16**:1104-1120 (Sept.) 1932.

66. Yakovlev, P. I., and Guthrie, R. H.: Congenital Ectodermoses (Neurocutaneous Syndromes) in Epileptic Patients, Arch. Neurol. & Psychiat. **26**:1145-1194 (Dec.) 1931.

67. Brouwer, B.; van der Hoeve, J., and Mahoney, W.: A Fourth Type of Phakomatosis: Sturge-Weber Syndrome, Amsterdam, Uitgevers-Maatschappij, 1937.

Pial lipoma probably arises because of local failure of normal control over formation of fat from the normally present pericapillary mesenchymal cells. In these cells, which have fat-forming potentialities, a panniculus adiposus of the pia proceeds to develop. Whether this is neoplastic or is a "malformation," or whether there is any difference between the two, is an open question.

Extradural lipoma seems to be related to a vague defect of the primitive fat-forming tissue itself.

Neither form of lipoma is related to meningioma.

There is a close relation between lipoma and angioma. Intraspinal lipoma appears to be related to neurofibromatosis and the other "phacomatoses."

Congenital defects are rather often associated with intradural lipoma. Obesity and multiple lipoma occasionally accompany the extradural lipoma.

NOTE.—Since the preparation of this paper, an additional case of intraspinal lipoma has been reported from the Mayo Clinic.[68]

68. Ehni, G. T., and Pugh, D. G.: Intraspinal Lipoma, Proc. Staff Meet., Mayo Clin. **19**:513-515 (Oct. 18) 1944.

The Mayo Clinic.

PHENOMENON OF VISUAL EXTINCTION IN HOMONYMOUS FIELDS AND PSYCHOLOGIC PRINCIPLES INVOLVED

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AND
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During World War I a variety of syndromes due to cerebral injuries were described. Among the numerous interesting signs noted was one of "visual inattention in homonymous fields," or "hemianopsic weakness of attention." Poppelreuter [1] observed 7 cases in which the patient was able to perceive only one of two figures or points simultaneously exposed on the sides of a central point of fixation. However, if only one figure was exposed in the "affected field," the image was seen. Head [2] noted this phenomenon in a case of a gunshot wound of the left occipitoparietal cortex, with residual aphasia and a right homonymous field defect, but his description lacks details. Riddoch [3] reported 2 cases of defective attention in the right homonymous fields, and in both instances there was a neoplasm in the angular and supramarginal gyri on the left side. Akelaitis [4] described 2 cases of left and 1 case of right homonymous hemiamblyopia due to head trauma in which attentiveness, as tested by Oppenheim's method, was impaired. Oppenheim [5] suggested that the patient's "attentiveness" be tested by simultaneous exposures to objects at identical points in each homonymous field because some patients fail to appreciate the image on one side, although they could see it if it were exposed alone in the same position.

All these authors assumed that this visual symptom was due to lack of attention on the affected side. Their descriptions are relatively meager, and, as Head stated,[2] "these changes have not been completely investigated." Kluver,[6] in an extensive review of this and allied visual disturbances, made the same intimation. Recently we have studied a case of this type over a long period, and, after careful and detailed observation, we have found that the failure to appreciate an image on one side, as tested by Oppenheim's method, is not due to inattention but is the result of underlying normal psychologic mechanisms. This case and the psychologic principles involved are now reported.

REPORT OF A CASE

A Marine aged 29 was wounded in the right side of the head but was not incapacitated until a missile struck him in the left occipitoparietal region, when he fell unconscious. When he regained consciousness, he found himself in a dugout, unable to speak or move the right side of the body. He was evacuated to a hospital. On examination global aphasia, right hemiplegia and apparent hemianopsia were noted. One week later the hemiplegia had disappeared. A craniotomy was then performed, and fragments of bone were removed from the left side of the head. The underlying occipitoparietal cortex was contused. The patient continued to improve. Within a month the hemianopsia began to recede, and he became more communicative. However, the following significant symptoms lingered during the next two months: (*a*) severe acalculia, (*b*) spelling defect, (*c*) dysgraphia and (*d*) inability to perceive an object on the right when a concomitant stimulus was present in the left field of vision. Spontaneous speech returned. He showed little agrammatism and no anomia. There was no finger agnosia or disorientation for right and left. His greatest defect was in calculation. He had always considered himself good in arithmetic, but twelve weeks after the injury he still was unable to recite the multiplication tables of 2's and 3's accurately. He made errors in simple tests, such as 8 plus 3 and other sums which equated to less than 20. The calculation defect was most marked for subtraction. Often he was unable to recognize the correct solution to the problem even when it was given to him, and he was seldom certain of the answer.

Visual Disturbances.—Ever since the hemianopsia had begun to recede, the patient complained, "If I stare long enough, my vision starts to blur on the right side.

From the United States Naval Hospital, San Diego, Calif.

Presented at the Seventieth Annual Meeting of the American Neurological Association, New York, May 20, 1944.

1. Poppelreuter, W.: Die psychischen Schadigungen durch Kopfschuss im Kriege 1914-1916: Die Störungen der niederen und hoheren Schleistungen durch Verletzungen des Okzipitalhirns, Leipzig, Leopold Voss, 1917, vol. 1.

2. Head, H.: Aphasia and Kindred Disorders of Speech, London, Cambridge University Press, 1926, vol. 1, p. 439; vol. 2, p. 108.

3. Riddoch, G.: Visual Disorientation in Homonymous Half-Fields, Brain **58**:376-382, 1935.

4. Akelaitis, A. J.: Studies on the Corpus Callosum: V. Homonymous Hemiamblyopia Before and After Section of the Corpus Callosum, Arch. Neurol. & Psychiat. **48**:108-118 (July) 1942.

5. Oppenheim, H.: Diseases of the Nervous System, translated by E. E. Mayer, Philadelphia, J. B. Lippincott & Co., 1900, p. 59; Lehrbuch der Nervenkrankheit, ed. 7, Berlin, S. Karger, 1923, p. 1113.

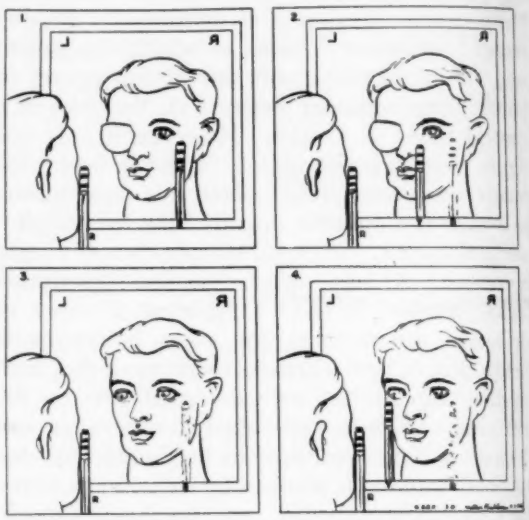
6. Kluver, H.: Visual Disturbances After Cerebral Lesions, Psychol. Bull. **24**:316-358, 1927.

I can't go to the picture show for the same reason. When I first start to read, everything is clear, but then I must stop because the right side blurs. After a rest I can see again. Also, if I look at one object long enough and look away, I still can see it." The last phenomenon was present for one month. Examination revealed that the patient was unable to see in his right homonymous field when an object was exposed simultaneously in the left field of vision. This was true with both uniocular and binocular testing. When the perimetric fields became normal (the last defect noted was for color in the right inferior quadrant) this phenomenon became most apparent. While he was fixating on a central point, the patient clearly perceived the form and color of an object placed in his right field of vision. However, when another object was brought into view on his left side, the image on the right became extinct. This extinction phenomenon was noted on repeated examinations in the right homonymous fields of vision. During the extinction of the image the patient made a strong effort to "see" the object by squinting his eyes and concentrating, but was unsuccessful. However, as soon as the stimulus in the left field was removed, he perceived the exposed object on the right. When tested for separately, the object on the right appeared clear, but sometimes blurred and dull. The object seemed to fluctuate in distinctness.

In time the remaining aphasic symptoms decreased further, although the acalculia was still striking. The visual phenomenon began to change. Fourteen weeks after the injury it was noted that the image in the right field did not always vanish when the left field was stimulated. Instead, it became dull, lost its form and color and appeared shadowy. There was no micropsia or teleopsia. Again, when the stimulus in the left field of vision was removed, the object on the right became more luminous and regained its color and meaning. This was noted irrespective of the degree of likeness or unlikeness in luminosity of the objects exposed in the opposite fields of vision. There was no apparent loss of attention. What there seemed to be was a relative reduction of visual acuity or an obscuration of the visual image (obscuration phenomenon). These phenomena were less apparent the nearer the object in the right field was exposed to the point of fixation.

Sixteen weeks after the injury the following observations were noted: (*a*) On separate tests of all four quadrants, the patient claimed that the image in the right superior homonymous field of vision was clearer than that in the right inferior homonymous field. (*b*) The obscuration phenomenon was much more apparent in the inferior than in the superior quadrant on the right side. Thus, when a pencil was placed in the patient's right inferior field he recognized it, but when another pencil was placed in his left niferior field the one on the right became blurred, dull and shadowy. The same was true when the corresponding superior quadrants were tested, but the difference here was much less apparent than in the comparable lower quadrants. When a long pencil was held vertically in the right field of vision, the patient stated he perceived that part of the pencil in the upper quadrant more clearly than the portion in the lower quadrant. The simultaneous exposure of an object in the same position on the left side produced a further decrease of perception on the right side, particularly in the lower quadrant.

Five months after the injury[7] the patient complained that "on looking in a mirror the right side of my face is sort of blurred. My right eyeball is not clear; but when I cover my left eye, I can see the right eye clearly in the mirror. I can also see the right side of my forehead better than the right side of my jaw." These visual disturbances were well demonstrated by requiring the patient to fixate with one or both eyes in a mirror 30 inches (76 cm.) away under daylight illumination. The test object used in the right lower field of vision was a red pencil placed vertically on the cheek below the outer canthus of the right eye (figure). The detailed observations made under these conditions are listed in table 1. In summary, it appeared that the greater the stimulation in the left fields of vision, the less the patient saw on the right. There was obscuration of form; with sufficient stimulation in the left field even motion could not be perceived on the right.



What the patient sees in the mirror (responses under conditions 1 to 4 in table 1). The red pencil is designated by *R*, and the yellow pencil, by *Y*. The patient fixates on one or both eyes and is asked to describe the perceived reflected image of pencils held on one or on both sides of the fixation point. Mirror images of *R* and *L* represent the right and left sides of the patient's body. Note that the more stimulation there is in his left field of vision, the more blurred does the image (pencil *R*) in the right field of vision appear to him.

An interesting observation was the variability of the image perceived in the right field of vision. This fluctuation at times was so pronounced that the results obtained during special visual tests were confusing. However, when these variations in perception were timed, a definite periodicity in fluctuation was noted, as shown in table 2.

7. At this time, when the patient returned from a forty day furlough, he complained that he did not know "what the right hand was doing." Detailed examination of the cutaneous sensory status revealed the following disturbances in his right upper extremity: (1) unawareness of the extremity; (2) fluctuating sensory defects; (3) decrease of cutaneous sensory perception on the right side when the left hand was stimulated simultaneously (cutaneous sensory extinction phenomenon); (4) reduction of sensory adaptation time over the entire right side of the body, and (5) absence of after-sensation on the same side.

TABLE 1.—*Data on Visual Fixation Tests*

Condition	Response
1. Right eye fixated in mirror; left eye closed; red pencil placed on right cheek	Red pencil appeared clear, but image fluctuated in distinctness (table 2)
2. Right eye fixated in mirror; left eye closed; red pencil on right cheek and yellow pencil placed on the nose	Red pencil appeared blurred, but details were still discernible; image of red pencil fluctuated in distinctness and color
3. Binocular fixation in mirror; red pencil on right cheek	Red pencil appeared blurred; details were imperceptible; distinctness of image waxed and waned periodically
4. Binocular fixation in mirror; red pencil on right cheek; yellow pencil on left cheek	Red pencil appeared very blurred, becoming brown and and gray; no details; fluctuation phenomenon apparent, image often disappearing completely
5. Binocular fixation in mirror; red pencil on right cheek; three yellow pencils on left cheek	Form of red pencil was barely recognized; color was imperceptible; notable fluctuation in acuity; at times image and appreciation of movement disappeared; images of pencils on left side clear and nonfluctuant

each eye saw an after-image. However, simultaneous or rapidly successive light stimulation of both eyes (an illuminated vertical line thrown in one eye and a round light in the other) produced a persistent after-image, usually in the left eye. Rarely were there after-images in both eyes at the same time or only in the right eye.

Tachistoscopic Examination: This test, performed seven months after the injury, showed reduction of perception in the right side of the field when the image was exposed for less than one second.

Color Tests: The patient could recognize colors in each of the field quadrants. However, the simultaneous exposure of objects in the two half-fields of vision caused disappearance of the color on the right side (figure). The degree of change depended on the intensity of visual stimulus thrown in the normal field. The more visual stimulus there was on the left side, the less color the patient perceived on the right side. In all instances color ultimately changed to gray. Red became brown and then dark gray, while yellow changed to light gray. On prolonged fixation on a black object, such as the center of a black cross, the part which was in the right and lower field of vision

TABLE 2.—*Fluctuation in Perception of Image from Right Lower Field of Vision with Patient Fixating an Eye in a Mirror Under Conditions Indicated in Columns A to D**

	A: Binocular Test; Red Pencil on Right Cheek		B: Right Uniocular Test; Red Pencil on Right Cheek		C: Right Uniocular Test; Red Pencil on Right Cheek and Two Yellow Pencils on Left		D: Binocular Test with Simultaneous Stimulation; Right Red Pencil, Left Two Yellow Pencils	
	Time	Duration	Time	Duration	Time	Duration	Time	Duration
Clear	9	4	3	5	..	..	..	..
Blurred	12	22	8	8	3	4	7	9
Clear	35	7	16	6	7	5	16	6
Blurred	42	11	22	9	12	9	22	4
Clear	53	7	31	7	21	4	26	4
Blurred	60	15	38	27	25	16	30	4
Clear	75	31	65	12	41	11	34	4
Blurred	106	24	77	21	52	19	38	7
Clear	130	34	98	11	71	4	45	13
Blurred	164	..	109	8	75	7	58	11
Clear	..	..	117	17	82	11	69	11
Blurred	..	..	134	9	93	..	80	1
Clear	..	..	143	7	..	..	81	8
Blurred	..	..	150	11	..	..	89	8
Clear	..	..	161	..	..	..	97	9
Blurred	..	..	..	..	..	..	106	..

* The conditions indicated in columns A to D are similar to the conditions of the tests shown in table 1. Here, time and duration of clearness or blurring of image are expressed in seconds.

The patient volunteered the information that the image seemed to change faster as the test continued. The blurred image seemed to last longer than the clear image, but this phenomenon was variable. The image was much clearer when it was near the center.

Special Visual Tests.—Perception of Form and Contour: These functions were normal. Localization in space, ability to fuse images and stereoscopic vision were also intact. When the patient was asked to scrutinize at the Schröder staircase illusion,[8] he could see each figure in reversible perspective. As he continued to fixate on the staircase with one or both eyes, the figure continued to reverse itself at a speed similar to the fluctuation rate observed for the right field of vision and as recorded in table 2.

Visual Imagery and Memory: These functions were intact, although at times the patient could not recall the color of tea and of certain animals.

After-Imagery: Uniocular after-imagery tests disclosed normal responses. When examined separately, appeared lighter than black and tended to become gray. Again, while he was fixating on a white cross, the part in the right and lower field became darker than white and approached a gray. Thus, all colors tended to fade and ultimately to change to gray. At times the right horizontal bar of the cross disappeared entirely, and the resultant image was not recognized as a cross. In this sense the gestalt of the exposed object was altered, even though one-half the cross was located in the normal field. All the visual phenomena noted in the affected fields of vision showed notable fluctuation in perception of the form and color of the image.

Displacement of Image: On his figuring columns of numbers, the patient tended to look at the rows to his left. Thus, on adding upward, he noted that the numbers in the upper part of the 10's column were displaced by the adjacent numbers in the 100's column, and then by those in the 1,000's column. On other occasions he noted that after he finished writing a line the first few words were displaced to the right and down, so that the line of words appeared crooked. These displacements appeared to be types of spatial

8. Woodworth, R. S.: Experimental Psychology, New York, Henry Holt & Company, Inc., 1938, p. 696.

disorientation. There was no ring scotoma or diplopia in the homonymous fields, as suggested by Goldstein.[9]

Opticomotor Nystagmus: This phenomenon, elicited by the patient's staring at a revolving vertically striped drum, was present bilaterally, but the quick component was more pronounced to his left.[10]

Ocular Dominance: Alinement and other methods showed that the patient was right eyed.

Muscle Balance: The Maddox rod test showed a 1 degree of esophoria and 0.5 degree of right hyperphoria for distance; 4 degrees of exophoria and 0.5 degree right hyperphoria for near point.

Psychologic Examinations.[11]—Three months after his injury the following features were noted: 1. Indications of an average pretraumatic intellectual level, inferred from average performances in the vocabulary and information tests. 2. Defective performances on retention tests involving speech as the motor response and symbolic material as the content to be retained (digit span and Wells-Ruesch object memory test). However, the performance was adequate on a retention test involving drawing as the motor response and nonsymbolic material as the content to be retained (Benton visual retention test). 3. Adequate abstract reasoning ability in a nonlanguage test (Weigl test). 4. Inferior performance on a test of visual analysis and synthesis (Kohs block designs test). 5. Small number of fairly accurate responses, with failure to interpret two plates, in the Rorschach performance. Five of the ten responses were of the "popular" variety. There were no color responses, but one human movement response was given. The total pattern was similar to the constricted performances described by Harrower-Erickson [11a] for a patient with cerebral tumor.

Psychologic reexamination seven months after the patient's injury showed the following features: (*a*) persistence of defective performance on the digit span test, moderate improvement in the Wells-Ruesch object memory test, which performance, however, was still below the average level, and adequate performance on an alternative form of the Benton visual retention test; (*b*) notable improvement in performance of the Kohs block designs test the patient now performing on a superior level and indicating considerable restoration of visual and analytic-synthetic capacity, and (*c*) no essential change in the Rorschach performance, the same picture of constriction being shown.

COMMENT

Since the injury the patient has shown progressive restitution of visual function. The first sign of recovery was the recession of the right homonymous hemianopsia for motion, color and form. This occurred from the center toward the periphery, and the rate of recovery has been slightly more rapid in the upper quadrants. As these retrograde changes took place other visual disturbances, which are not recognized with ordinary tests, became apparent. The patient sensed the disturbances while reading or looking at motion pictures, and it was these complaints which prompted us to investigate the visual functions in great detail. Although routine perimetric examination seemed to indicate preservation of vision in each field, the simultaneous exposure of objects on the two sides of a fixation point caused the image perceived from the right field to become extinct. Later the extinction phenomenon was replaced by obscuration and still later, by blurring or dulling of the image. These phenomena have been more apparent in the right homonymous inferior quadrants. The image in the right field of vision appeared to fluctuate in clearness of form and intensity of color.

The phenomena of visual extinction, obscuration and dulling seem to be unusual, since they have rarely been observed or reported. This may be due to the fact that few examiners search for these defects, and, as previously noted, the usual neurologic tests will not disclose them. Poppelreuter [1] and others noted one of these phenomena, namely, that of extinction, and explained it on the basis of disturbance in visual attention. The act of perceiving simultaneously exposed objects in zones equidistant from a fixation point requires the normal person to concentrate on three different foci, and his attention must necessarily be divided. Under pathologic conditions a disturbance in the attention mechanism in homonymous fields of vision may occur. Thus, Poppelreuter [1] found that only one of two figures concomitantly exposed on each side of a fixation point could be seen by the patient. However, when the "active attention" of the patient was directed toward the affected field, the patient could see both figures simultaneously. Poppelreuter [1] did not state whether or not the latter observation was a consistent one in his cases. In our case the image in the affected field fluctuated. There were alternate extinction and blurring during the "double exposure" testing. At times it seemed as though the patient could see the object if he "concentrated," but this appeared to be due to a "fluctuation" mechanism which is normally present,[8] and not to an increase or a decrease in attention.

It is probable that weakness of attention is one factor in the elicitation of the extinction phenomenon. Newhall,[12] in controlled experiments,

9. Goldstein, K.: Ueber monokuläre Doppelbilder. Ihre Entstehung und Bedeutung für die Theorie von der Funktion des Nervensystems, Jahrb. f. Psychiat. u. Neurol. **51**:16-38, 1934; Aftereffects of Brain Injuries in War, New York, Grune & Stratton, Inc., 1942.

10. Strauss, H.: Ueber die hirnlokalisatorische Bedeutung des einseitigen Ausfalls des optikinetischen Nystagmus und der hemianopischen Aufmerksamkeitsschwäche, Ztschr. f. d. ges. Neurol. u. Psychiat. **143**:427-435, 1933.

11. Performed by Lieutenant Commander A. L. Benton, H(V)S, U.S.N.R.

11a. Harrower-Erickson, M. R.: Personality Changes Accompanying Cerebral Lesions (Rorschach Studies of Patients with Cerebral Tumor), Arch. Neurol. & Psychiat. **43**:859-890 (March) 1940.

12. Newhall, S. M.: Effects of Attention on the Intensity of Cutaneous Presence and on Visual Brightness, Arch. Psychol. (no. 61) **9**:1-75, 1923.

found that the closer the attention the better discrimination there is between faint stimuli and no visual stimulus. Still, it does not appear that the attention mechanism alone would account for the visual extinction, obscuration or color-dulling phenomena. Goldstein [13] also expressed the opinion that these phenomena are not due to lack of attention. He proposed the theory that the cause of these different reactions may be due to "lability of threshold" in a damaged cortex, which needs more energy than the normal. The nerve energy in the organism is a constant, and the normal cortex, he stated, tends to use the available energy to such an extent that the remaining energy is not sufficient to stimulate the diseased cortex to effect a performance. Granted the correctness of this theory, one must, however, take into consideration the rivalry and dominance mechanisms in explaining the extinction and associated phenomena. Rivalry and dominance are normal psychologic processes and can be detected only with special tests. Sherrington [14] demonstrated the existence of rivalry between the images perceived by the two eyes, or half-retinas. Breese [15] and others showed that stimuli arising from the two fields of vision are in constant competition with each other. Light intensity, presence of figures or movements of the object exposed influence the subject's ability to visualize the images in the two fields equally: (*a*) The brighter the exposed field, the more visible it is 60 per cent of the time; (*b*) a field containing lines prevails over a plain field as much as 70 per cent of the time, and (*c*) when both fields contain figures and the one figure in one field is made to move, it remains in sight more than half the time.

Rivalry, dominance and attention mechanisms are normal psychologic processes which operate at all times and are a function of the cortex. The visuosensory cortices are in competition with each other and are in equilibrium when at rest. If one cortex is diseased, as it was in our patient, the visual stimuli coming to that side are not as well integrated as those coming to the normal side. The affected cortex does not possess the nerve energy as does the normal cortex, or the capacity to use it when the incoming stimuli are increased. Consequently, there must be a difference in perception, and this difference is made more conspicuous by the rivalry and dominance mechanism. Hence, when there are no new or strong stimuli in the normal field of vision, there is no appreciable decrease in perception of an object held in the pathologic field. The available "energy" is sufficient for the diseased cortex to function, and there is little competition between the two sides. However, if stimuli are thrown into the intact field, the rivalry mechanism becomes apparent. The function of the defective cortex is dominated by the normal part of the brain, and there results a relative decrease in acuity and light intensity in the affected field of vision, leading to the phenomena of dulling and obscuration. The rivalry and consequent dominance of the normal over the pathologic side may be so pronounced as to cause complete extinction of the form, color and movement of the image perceived from the affected field. It has been found that the more the normal half is stimulated, the less the affected half perceives.

Such competition may under certain conditions interfere with the patient's proper visual perception. It is known that the perceptual consciousness of an object is the effect of integrated stimuli in which the total stimulus pattern is related to the total reaction pattern through a unified neural mechanism. If the rivalry between sensations arising from the opposite lateral fields of vision becomes pronounced, as in reading or looking at motion pictures, the images coming from the affected fields of vision blur, and the patient's total visual perception becomes impaired. Similar competitive mechanisms have been noted between the cutaneous sensations on the two sides of the body in the patient described in this report, in patients with lesions of the parietal cortex (personal observations) and between certain reflexes, as demonstrated by Sherrington.[16]

SUMMARY

In a patient with a gunshot wound of the left occipitoparietal cortex, various psychologic mechanisms became apparent during the advanced stages of restitution of visual function from right homonymous hemianopsia. Visual stimuli originating in the normal homonymous field of vision tended to suppress or obscure the image originating simultaneously in the opposite, affected, field of vision. The more stimulation there was in the normal field, the less the patient saw in the pathologic field of vision. The affected field showed fluctuation of sensation. Rivalry, dominance and attention mechanisms are considered as explanatory principles.

13. Goldstein, K., in discussion on Phenomenon Visual Extinction in Homonymous Fields, Tr. Am. Neurol. A., 1944, to be published; personal communications to the authors.

14. Sherrington, C.: On Binocular Flicker and the Correlation of Activity of Corresponding Retinal Points, Brit. J. Psychol. **1**:26, 1904.

15. Breese, B. B.: Binocular Rivalry, Psychol. Rev. **16**:410-415, 1909.

16. Sherrington, C.: Intergrative Action of the Nervous System, New Haven, Conn., Yale University Press, 1906.

MENTAL SYMPTOMS FOLLOWING HEAD INJURY

A STATISTICAL ANALYSIS OF TWO HUNDRED CASES

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BOSTON

PRESENT INVESTIGATION

METHOD

From a total of 430 patients with head injuries admitted to the Boston City Hospital between July 1942 and September 1944 a series of 200 was selected for study. Two hundred and thirty patients were eliminated because no adequate follow-up observations could be obtained, because the patients were under 15 or over 55 years of age or because they were vagrants or chronic alcohol addicts. The patients had all sustained recent injuries; they were seen on admission to the hospital, were closely followed during their stay in the hospital and were observed at intervals of two to three months thereafter. The present report deals with their post-traumatic mental symptoms and the relation of these symptoms to the other fields of investigation.

The group of examiners consisted of neurologists, psychiatrists, a psychometrist, an electroencephalographer and a social worker.

MATERIAL

Age, Sex and National Stock.—The age distribution of the 200 patients was as follows:

Age, Years	No. of Patients
15-19	36
20-29	48
30-39	42
40-49	51
50-55	23

There were 125 males and 75 females, and the following national stocks were represented:

Irish	77
English	29
Latin	21
Negro	13
Slavic	12
Semitic	12
German or Scandinavian	10
Other racial stocks	26

Occupation.—Skilled or semiskilled workers 96; Domestics or housewives 39; Students 20; Policemen, firemen, etc. 13; Common laborers 11; Other workers 21

Alcoholism.—For 143 patients there was no evidence of alcohol on admission; 53 had ingested alcohol but were not intoxicated, and 4 were intoxicated.

Manner of Injury.—The accidents could be classified as follows:

Traffic accidents	91
Industrial accidents	24
Fighting or robbery	24
Falls on street	16
Domestic accidents	15
Recreational accidents	12
Other types	18

Coma and Disorientation.—Twenty patients had no period of coma; 90 patients were comatose or semicomatose for less than ten minutes; 42 patients, for less than thirty minutes; 20 patients, for thirty to sixty minutes; 17 patients, for up to six hours; 5 patients, for six to twenty-four hours, and 4 patients over twenty-four hours. For 2 patients the duration of coma was uncertain but brief. One hundred seventy-three patients were disoriented for less than twelve hours; 4 patients, for twelve to twenty-four hours; 12 patients from one to seven days, and 11 patients, over seven days.

In accordance with general usage, the period of coma was judged by the absence of response to stimulation. The period of disorientation was usually recorded by disorientation in time. The duration of post-traumatic amnesia and retrograde amnesia was recorded on the patient's follow-up visit to the clinic when the amnesia had reached its stable minimum. The presence or absence of complicating factors, such as litigation or occupational and financial difficulties, was recorded without reference to their possible bearing on the development of post-traumatic mental complications.

Type of Injury.—Seventy-five patients had minor abrasions or hematoma of the scalp; 75 patients, laceration of the scalp and 6 patients, laceration with compound fracture. Thirty-five

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The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the President and Fellows of Harvard College.

patients had injuries to the limbs, and 24 patients had other or multiple injuries, in addition to the head injury. Evidence of fracture of the skull was present in 34 patients. Nine had cranial operations other than scalp suture, and 13 had operations of other types. One patient had both cranial and other operations.

The type of head injury represented by this material is therefore representative of those encountered among patients admitted to any general hospital and may be categorized predominantly as "closed head injury."

Length of Follow-Up Observation.—One patient was observed one month; 1 patient, two months; 48 patients, four to six months; 107 patients, six to nine months; 18 patients, nine to twelve months, and 25 patients over one year.

STATISTICAL EVALUATION OF MATERIAL

In evaluation of post-traumatic mental symptoms the mental condition immediately following an injury must be distinguished from that during the later part of the course. Any person might be impressed by a violent injury which may have brought him to the verge of death and may have resulted in injury and death to others and in loss of property to a varying degree. Such an emotional reaction might be expected normally to be at its height immediately after the injury, after which it would steadily subside. Outwardly, however, 133 of the 200 patients (67 per cent) gave an impression of calmness and cooperativeness; 20 were apathetic; 7 were excited; 16 had a severe emotional reaction, and 24 were confused.

Post-traumatic mental symptoms may be related to structural lesions or may be psychogenic. Some psychologic phenomena are known to be caused by structural lesions. For instance, this is the case with patients suffering from dysphasia or confabulations. The purpose of this study was to evaluate mental symptoms according to their correlation with all the other physical and mental factors of the head injury. The analysis is therefore of the patient's symptoms (complaints) in order that all possible objectivity may be maintained. Early in our experience my colleagues and I found that these complaints tended to fall into a limited number of categories, symptoms of anxiety, nervousness and fatigue emerging as leading factors, especially in the production of disability. The incidence of these mental symptoms during convalescence is given in table 1. It will be noted that by far the largest group of patients (48 of 70) fell into the category of those showing anxiety and fears, symptoms which were present more than twice as often as all the others combined.

It would be a misunderstanding to conclude from table 1 that the symptoms of fatigue and nervousness were present in only 7 and 4 patients respectively. Fatigue and nervousness were present, in addition to fears and anxiety, in practically every patient who presented the latter symptoms. Patients whose "predominant mental symptom" was fatigue or nervousness were persons in whom no anxiety reactions were present. On the other hand, the symptoms of the acute post-traumatic anxiety neuroses included syndromes such as acoustic hypersensitivity, periodic irritability, fatigue, disturbances in sleep and anxiety dreams, anxiety being the primary and predominant feature of these secondary character changes. There was no case of hysteria among our patients.

The symptoms of headache and dizziness are not taken into account in our psychiatric diagnoses.

TABLE 1.—*Predominating Post-Traumatic Mental Symptoms*

	No. of Patients
None	130
Fatigue	7
Nervousness; inability to concentrate	4
Fears; anxieties; panics	48
Depression; apathy	1
Hypochondriasis	2
Obsessive-compulsive neurosis	1
Hysteria	0
Personality change only	6
Hypomania; euphoria	1
Total	200

PRETRAUMATIC FACTORS ASSOCIATED WITH HIGH AND LOW INCIDENCES OF POST-TRAUMATIC MENTAL SYMPTOMS (TABLES 2 AND 3)

Age.—Of the patients of the oldest group (50 to 55 years), 51 per cent manifested mental symptoms, as compared with an average of 31 per cent of all patients and of only 15 per cent of the youngest group (15 to 19 years). No notable difference in occurrence of post-traumatic mental symptoms could be found in the intervening age groups.

Marital Status and Sex.—More women had mental complications than men, with a negligible difference between the incidence for married women and that for single women. However, fewer single than married men had mental complications.

Anxiety symptoms were present four times as often as all other mental symptoms combined in men, whereas in women anxiety symptoms were less than three times as frequent as fatigue and nervousness combined.

National Stock.—In 50 per cent of the patients of Latin and Slavic stock mental com-

plications developed, whereas only 17 and 21 per cent of the African and Irish patients respectively presented psychologic difficulties. There was a fairly even distribution among the other racial stocks, some of which, however, presented numbers too small for statistical evaluation.

Type of Accident.—By far the highest incidence of mental complications was found among the patients who had suffered industrial accidents. Only 1 of the patients who had sustained their head injuries during recreational activities and only 2 of the patients who had suffered injuries during domestic activities presented mental symptoms.

TABLE 2.—*Miscellaneous Pretraumatic Factor Associated with Low Incidence of Post-Traumatic Mental Symptoms*

	No. of Patients	Post-traumatic Mental Symptoms, %	No Post-traumatic Mental Symptoms, %	Personality Change Only, %
All patients	200	31.5	65.0	3.5
Age, yr.				
15-19	36	15	85	
Sex and marital status				
Male; single	45	14	86	
National stock				
African	13	17	83	
Irish	77	21	79	
Alcoholism on admission				
Intoxicated, or previous alcoholic ingestion	57	12	88	
Type of accident				
Recreational	12	8	92	
Domestic	15	13	87	

TABLE 3.—*Miscellaneous Pretraumatic Factors Associated with High Incidence of Post-Traumatic Mental Symptoms*

	No. of Patients	Post-traumatic Mental Symptoms, %	No Post-traumatic Mental Symptoms, %	Personality Change Only, %
All patients	200	31.5	65.0	3.5
Age, yr.				
50-55	23	51	49	
Sex and marital status				
Female; single and widowed	40	45	55	
National stock				
Slavic and Latin	38	50	50	
Occupation				
Policemen and firemen	13	58	42	
Alcoholism on admission				
No evidence of ingestion of alcohol	143	39	61	
Type of accident				
Industrial	24	55	45	
Manner of injury				
Struck by vehicle	45	50	50	
Pretraumatic psychiatric evaluation				
Preexisting anxiety; hypochondriasis; depression	21	57	43	

Occupation.—The highest incidence of post-traumatic mental symptoms was observed among policemen and firemen. Next to the frequency for this group was the incidence for the common laborers. The large group of patients classified as skilled and semiskilled workers presented an average incidence of mental complications.

Alcoholism on Admission.—In only a few patients with a history of ingestion of alcohol previous to injury did post-traumatic mental difficulties develop.

Psychiatric Family History.—The incidence of post-traumatic mental complications was highest among the patients with psychotic family members. On the other hand, it was low among the patients who had alcohol addicts and other types of psychopaths in their families. However, the numbers are too small to be of statistical significance.

Pretraumatic Psychiatric Evaluation.—The highest incidence of mental symptoms prevailed among patients with preexisting symptoms of anxiety, hypochondriasis and depressive neuroses. Next to this group came patients with preexisting general nervousness, in half of whom mental complications developed. Not all types of patients with preexisting neuroses reacted in this way, however. For instance, of the 5 patients with previous hysterial episodes, only 1 manifested psychiatric difficulties.

POST-TRAUMATIC FACTORS (TABLES 4 AND 5)

The difference between the incidence of post-traumatic mental symptoms for patients who sustained injuries in addition to those of the head and the incidence for patients who had head injuries only was negligible. The largest percentage of post-traumatic mental symptoms was found, however, among patients with additional injuries to their legs, whereas injuries to the face, chest, abdomen and arms each carried a comparatively low incidence.

Duration of Stay in Hospital.—Fewer patients who remained in the hospital for from four to seven days presented mental symptoms than did the patients who remained in the hospital for longer than fourteen days. The incidence of mental symptoms in patients who stayed less than four days was within the average range.

Post-Traumatic Headache and Dizziness.—The incidence of post-traumatic mental symptoms was high in patients who suffered from post-traumatic headache or dizziness. The incidence was highest for patients whose headache and/or dizziness lasted more than two months, whereas there was an average incidence of mental complications among patients for whom the duration of headache and/or dizziness was less than two months.

Associated Symptoms Immediately Following Injury.—Many patients who had both headaches and dizziness immediately after injury presented psychiatric complications, while patients who had none of these symptoms while in the hospital had a low incidence of mental symptoms.

TABLE 4.—*Miscellaneous Post-Traumatic Factors Associated with Low Incidence of Post-Traumatic Mental Symptoms*

	No. of Patients	Post-traumatic Mental Symptoms, %	No Post-traumatic Mental Symptoms, %	Personality Change Only, %
All patients	200	31.5	65.0	3.5
Duration of coma				
No coma or dazed state.	20	15	85	
Duration to recovery of complete orientation				
No measurable disorientation	18	16	84	
Post-traumatic amnesia				
No post-traumatic amnesia	17	12	88	
Associated symptoms immediately following injury				
None	63	19	81	
Signs of injury				
Minor abrasions of face or scalp	31	19	81	
Injuries other than those involving head				
Injury to face, chest, abdomen or back	35	20	80	
Injury to arm	24	21	79	
Duration of stay in hospital				
4-7 days	33	21	79	
Post-traumatic headache				
No headache	119	13	87	
Headache localized to side other than injury	15	20	80	
Post-traumatic dizziness				
No dizziness	127	15	85	
Post-traumatic dreams				
No dreams	75	5	95	
Measured post-traumatic intelligence				
Above normal intelligence	21	24	76	
Complicating factors, regardless of influence on post-traumatic course				
No complicating factors	72	6	94	

RESULTS OF POST-TRAUMATIC LABORATORY AND PHYSICAL EXAMINATIONS

Cerebrospinal Fluid.—Of the 7 patients with personality changes, 6 had a bloody spinal fluid, with a pressure above 200 mm. On the other hand, no correlation was found between the pressure and the content of blood of the spinal fluid and the development of the remaining psychogenic mental symptoms.

Blood Pressure During Later Part of Hospitalization or on Follow-Up Observation.—No correlation between the blood pressure and the incidence of post-traumatic mental symptoms was apparent.

Electroencephalographic Changes.—No correlation existed between the character or the severity of the electroencephalographic abnormality and the incidence or duration of post-traumatic mental symptoms.

Roentgenographic Changes.—Only 13 patients in the series gave roentgenographic evidence of fracture of the skull, and among these persons the incidence of post-traumatic mental symptoms was only slightly above the average.

Duration of Coma, Disorientation and Amnesia Following Head Injury.—Coma, disorientation and post-traumatic amnesia are all evidences of the initial disturbance of consciousness, and hence the immediate traumatic disorder of cerebral function. Whereas the frequency of mental symptoms did not vary to any considerable extent with the duration of coma, there was a low incidence of psychiatric complications among patients in whom no complete loss of consciousness had occurred. It was also noted that patients without measurable disorientation had a low incidence of mental symptoms. Variations in duration of disorientation, when present, had no significant influence on the frequency of mental symptoms. Likewise, only a small percentage of

TABLE 5.—*Miscellaneous Post-Traumatic Factors Associated with High Incidence of Post-Traumatic Mental Symptoms*

	No. of Patients	Post-traumatic Mental Symptoms, %	No Post-traumatic Mental Symptoms, %	Personality Change Only, %
All patients	200	31.5	65.0	3.5
Duration of coma				
More than 30 minutes	42	39	61	
Duration to recovery of complete orientation				
More than 12 hours	27	41	59	
Post-traumatic amnesia				
More than 2 days	22	41	59	
Associated symptoms immediately following injury				
Headache and dizziness	76	48	52	
Signs of injury				
Laceration of scalp	75	42	58	
Injuries other than those involving head				
Injury to lower limbs	17	48	52	
Immediate post-traumatic mental state				
Normal but severe emotional reaction	16	59	41	
Duration of stay in hospital				
More than 14 days	30	47	53	
Post-traumatic headache				
Any type	81	64	36	
Duration of headache				
More than 2 months	63	75	25	
Post-traumatic dizziness				
Any type	68	67	33	
Duration of dizziness				
More than 2 months	46	78	22	
Dreams				
Post-traumatic anxiety dreams	29	100	0	
Complicating factors, regardless of influence on post-traumatic course				
More than one factor	14	93	7	
Occupational difficulties.	11	73	27	
Pending litigation	34	59	41	

patients who had no post-traumatic amnesia presented mental complications, and there was no significant correlation between duration of post-traumatic amnesia, when present, and incidence of psychiatric symptoms.

Duration of Retrograde Amnesia.—Except for 8 patients, the retrograde amnesia was either of very short duration, not beyond a few minutes, or not present. Of the 8 patients, 4 had been intoxicated at the time of injury, and the remaining 4 patients suffered serious injuries, as expressed by fractures of the skull and long-lasting post-traumatic amnesia. It is interesting that in only 1 of the 8 patients with a retrograde amnesia of more than one hour did psychogenic symptoms develop. This patient was an alcoholic psychopath with a great many pretraumatic symptoms of anxiety whose preexisting psychiatric condition was slightly worse for three months after injury.

Time of Onset of Mental Symptoms as Compared with Time of Onset of Headache and Dizziness.—The onset of post-traumatic mental symptoms as compared with that of headache was later on an average. Of the 59 patients whose mental symptoms lasted longer than two months, the majority had an onset of mental complications during the first to the eighth week after leaving the hospital. On the other hand, of the 62 patients with post-traumatic headaches lasting more than six months, the great majority (41 patients, or 82 per cent) had headaches during hospitalization. Likewise, in the majority of patients (35, or 76 per cent) with post-traumatic dizziness of more than two months' duration the onset was during hospitalization.

Influence of Environmental Complications on Post-Traumatic Psychiatric Difficulties.—The presence or absence of environmental factors in convalescence was recorded regardless of their significance in the opinion of the psychiatrist. Problems in relation to litigation and compensation and occupation had a significant correlation with the development of post-traumatic mental symptoms, whereas social or sexual difficulties, as well as coexisting physical disease, influenced the psychiatric condition more seldom. In table 6 the data on these factors are presented in detail.

Closer investigation showed the influence of such complicating factors on all but 4 of the 63 patients with post-traumatic mental complications. It is interesting, however, to note that in only about one half to one third of all patients for whom complicating factors were noted did such a factor become associated with post-traumatic psychiatric difficulties. For instance, whereas litigation alone formed a complicating factor in the cases of 34 patients, it was correlated with mental difficulties in only 20 patients. With each patient it was not the complicating factor in itself, but the manner in which the patient reacted to the complication, before as well as after the injury, that was essential for the development or absence of post-traumatic mental complications.

TABLE 6.—*Complicating Factors Appearing in the Post-Traumatic Psychiatric Course* *

	No. of Patients	Post-traumatic Mental Symptoms, %	No Post-traumatic Mental Symptoms, %
None	72	6	94
Litigation, compensation	34	50	41
Diseases other than mental	28	32	68
Domestic and family troubles	18	33	67
More than one, including litigation	14	93	7
Occupational difficulties	11	73	27
Other financial problems	8	13	87

* Personality changes only were not included among the post-traumatic mental disorders.

COMMENT

Age.—The preponderance of mental complications in the older age groups is probably related to more frequent problems of occupational and financial adjustment.

Marital Status and Sex.—Occupational and financial problems, which are more pressing in the married state, probably favored the high incidence of mental difficulties among married males.

Type of Accident.—Evidently the compensation problem which is connected with industrial accidents, accidents which are followed most frequently by mental symptoms, is a strong contributing factor in the development of mental difficulties.

Occupation.—The high incidence of mental complications among policemen and firemen can probably be attributed to their attitude toward the hazards of their occupation, as occupational factors had no influence on the students, only a few of whom showed mental symptoms.

Effect of Alcoholic Intoxication on Admission.—The low incidence of post-traumatic mental symptoms in patients with a history of ingestion of alcohol previous to injury can be compared with the results of the investigation of the incidence of post-traumatic neuroses in victims of the Cocoanut Grove disaster.[1] Of the victims who had a long-lasting amnesia which blotted out parts or all of the terrifying events, only 19 per cent had a post-traumatic neurosis,

1. Adler, A.: Neuropsychiatric Complications in Victims of Boston's Cocoanut Grove Disaster, J. A. M. A. **123**:1098-1101 (Dec. 25) 1943.

whereas the incidence was 75 per cent for patients who had amnesia for less than five minutes or no amnesia. It can be assumed that the psychologic impression of the injury is less vigorous if the patient is under the influence of alcohol. In deeply intoxicated patients there is of course no memory of the injury at all. Actually, about one half of all persons with head injuries who had retrograde amnesias of longer than five minutes had been intoxicated at the time of injury.

Duration of Stay in Hospital.—Evidently prolonged stay in the hospital decreases the patient's chances to adjust probably because his thoughts become increasingly centered around his injury, which impresses him as more serious when his stay in the hospital is prolonged. On the other hand, an initial protective environment provided by a few days' hospitalization and reassurance from the physicians seems preferable to the regimen of having the patient leave the hospital within the first few days, so that he is thrown on his own resources in his readjustment.

Duration of Coma, Disorientation and Amnesia.—The low incidence of post-traumatic mental symptoms in patients who had no coma or disorientation might be explained by assuming that these patients felt that nothing serious had happened to them, an attitude which is helpful for future readjustment.

DESCRIPTION OF POST-TRAUMATIC PSYCHIATRIC SYNDROMES

The patients with mental symptoms could be divided into two groups: patients who had not shown psychiatric abnormalities previous to injury and patients whose pretraumatic psychiatric condition had grown worse through accentuation of previously existing symptoms or through the addition of new mental symptoms to those already present.

TABLE 7.—*Relation of Pretraumatic to Post-Traumatic Mental Symptoms* *

	Total No.	No. with Post-Traumatic Mental Symptoms
Patients with no abnormality in the pretraumatic personality	89	26 (29%)
Normal pretraumatic personality, but minor variants	31	9 (29%)
Patients with abnormal pretraumatic personality	71	26 (37%)

* In 9 patients the pretraumatic personality could not be evaluated because data were insufficient.

Table 7 reveals that only slightly fewer patients of previously normal personality (29 per cent) presented post-traumatic symptoms than did patients with pretraumatic psychiatric difficulties (37 per cent).

Of the 26 patients with normal pretraumatic personalities who had mental complications, symptoms of anxiety were present in 23, an incidence eight times that of all the other symptoms combined. On the other hand, in patients with previous psychiatric difficulties anxiety developed only two and a half times as often as all the other symptoms combined. It can therefore be stated that, particularly in previously normal patients, the type of psychiatric difficulty was predominantly the anxiety neurosis. The psychiatric syndrome in patients with pretraumatic mental difficulties varied to some extent through modification of previous liabilities.

POST-TRAUMATIC ANXIETY STATES

McCurdy [2] gave a thorough description of a type of acute post-traumatic anxiety neurosis which he named "anxiety state," a designation applied to this condition ever since. Roussy and Lhermitte [3] and Kardiner [4] described this condition among the neuroses of World War I. Literature concerning this subject gathered from observations made in the present war is growing rapidly (Blain,[5] Brosin,[6] Garmany,[7] Henderson and Moore,[8] Kubie,[9] Raines and Kolb,[10] Sagebill and Bird,[11] Symonds,[12] and Torrie.[13]) There is a striking uniformity of symptoms in

2. McCurdy, J. T.: War Neuroses, London, Cambridge University Press, 1918.

3. Roussy, G., and Lhermitte, J.: The Psychoneuroses of War, translated by W. B. Christopherson, London, University Press, 1918; Paris, Masson & Cie, 1918.

4. Kardiner, A.: The Traumatic Neuroses of War. Psychosomatic Medicine, Monograph II-III, New York, Paul B. Hoeber, Inc., 1941.

5. Blain, D.: Personal and Morale Factors in the Etiology and Prevention of Traumatic War Neurosis in Merchant Seaman, Am. J. Psychiat. **100**:131-135 (July) 1943.

6. Brosin, H. W.: Panic States and Their Treatment, Am. J. Psychiat. **100**:54-61 (July) 1943.

7. Garmany, G.: Reactive Anxiety and Its Treatment, Lancet **1**:7-9 (Jan. 1) 1944.

8. Henderson, J. L., and Moore, M.: The Psychoneuroses of War, New England J. Med. **230**:275-278 (March 9) 1944.

9. Kubie, L. S.: Manual of Emergency Treatment for Acute War Neuroses, War Med. **4**:582-598 (Dec.) 1943.

10. Raines, G. N., and Kolb, L. C.: Combat Fatigue and War Neurosis, U. S. Nav. M. Bull. **41**:1299-1309 (Sept.) 1943.

11. Sagebill, J. L., and Bird, L. C.: A Study of Psychiatric Casualties Received at the U. S. Naval Base Hospital—from the Solomon Islands Battle Area, U. S. Nav. M. Bull. **41**:1927-1937 (Nov.) 1943.

12. Symonds, C. P.: Anxiety Neuroses in Combatants, Lancet **2**:785-789 (Dec. 25) 1943.

13. Torrie, A.: Psychosomatic Casualties, Lancet **1**:139-143 (Jan. 29) 1944.

patients suffering from this condition. In the following discussion some features observed in our patients with head injuries are emphasized.

It was usual to find that patients were conscious that their fears and panics were related to the accident as such. For instance, persons who had suffered traffic accidents felt unable to cross a street or began to shake and had to cling to some one to lead them over. People who had been drivers of cars when the accident occurred were unable to drive again, and some had states of panic, with trembling and perspiring on the mere thought of doing so again. Firemen who had sustained their accidents during work trembled at the mere thought of going back to work, climbing ladders and fighting fires again. The sound of passing fire sirens threw them into panic states. Anxiety regarding the condition of the head was expressed by less than half these patients. Such persons expressed fear that they might become insane or paralyzed, that pressure on the brain might develop, that something in the head might be irreparably broken or that the memory might be permanently impaired. Reassurance from the physician alleviated, but did not cure, their anxiety state.

POST-TRAUMATIC NIGHTMARES

The anxiety state was further characterized by the occurrence of nightmares. Of 70 patients with mental symptoms, 39 suffered from post-traumatic anxiety dreams, 11 of these having had nightmares previous to injury also. Of the remaining 31 patients with mental symptoms, 18 had no dreams, and no information concerning dreams was obtained from the other 13. Of the 18 patients who had mental symptoms but no anxiety dreams, 7 had no neurosis but presented a personality change only, evidently related to structural changes of the brain. Two other patients had depressed emotions related to accompanying injuries of long duration. In 7 of the remaining 9 patients, the post-traumatic condition was a mere exacerbation of previously existing psychiatric liabilities. Only 2 patients with normal pretraumatic personalities had an anxiety condition which had developed after injury and which was not accompanied by anxiety dreams. One of these, a young woman, dreamed of seeing her dead father, although she had never dreamed of him before. The case was that of a clearcut "compensation neurosis," and the father's death had been of decisive influence on the patient's financial condition. This patient is still in the midst of litigation procedures for a large sum, although her injury was comparatively small. She takes an active and determined interest in the procedures, with all her anxieties centered around the compensation. The second patient, who, after his accident, was afraid of returning to his former occupation, which he had previously disliked because of associated danger, dreamed about his return to another, preferred type of work. He actually never returned to his former occupation and evidently had made up his mind not to do so rather soon, thus evading anxiety.

The patients regularly woke from the anxiety dreams with a start, trembling and perspiring. Only 4 of the 39 patients with post-traumatic nightmares had these dreams during the first few nights following injury. The dreams represented a reaction to the frightening experience, and thus they repeated the accident with hardly any distortion. For instance, a young laborer, who had been pushed by a car for some distance before hitting the pavement, relived the frightening experience in several anxiety dreams during the first few nights following the accident. The nightmares of the remaining 35 patients occurred after an interval during which they had sufficiently recovered to return home, usually during the first or second week at home. This delay indicates their anxiety in relation to their pending obligations, rather than merely a horror connected with the injury itself. Consequently, the dream content was distorted, and was concerned with mutilation and destruction, often with the patient bleeding. This delay is in contrast to the immediate occurrence of nightmares in patients who had gone through some harrowing experience which had dazed them to such an extent that for some time they were unable to deal with it on a conscious level. I [1] observed the immediate appearance of nightmares in 15 of the 25 patients who were subjected to the horrors of a disaster with burns and partial asphyxiation (Cocoanut Grove fire in Boston). These dreams also repeated incidents of the disaster with hardly any distortion of content.

Prolonged physical disability, such as that caused by accompanying injuries, occasionally brought about long delay in appearance of anxiety symptoms and anxiety dreams. For instance, in a patient who had been kept in bed for six months because of a fractured leg anxiety dreams developed only at the end of that time, together with other symptoms of anxiety, which then prevented him from returning to full work.

All 28 patients with post-traumatic anxiety dreams and no such dreams previous to injury also presented other symptoms of anxiety. Cases of this type have been reported by McCurdy,[2]

Kardiner [4] and Schilder [14] in their descriptions of patients suffering from post-traumatic anxiety neuroses.

It is interesting to note that none of the 8 patients with retrograde amnesia lasting more than one hour had anxiety dreams, but the number of patients is too small to justify definite conclusions.

The presence and prolonged duration of headaches and dizziness were noted two to three times as often in patients with post-traumatic nightmares as in the whole group of 200 patients.

ATTITUDE TOWARD EMPLOYMENT

In 8 of the 11 patients in whom occupational difficulties had been noted the attitude toward employment underwent a characteristic change after the injury. They had worked steadily before injury but had been laboring for some time under emotional stress in relation to their occupation, which they resented because of associated danger or monotony or because they felt unduly burdened. After injury this chronic tension developed into an acute exacerbation, which became incapacitating because of associated fears and other mental symptoms. This condition freed them from their obligations to continue their former occupation. The use of this mechanism of "secondary gain" is a part of the neurotic symptom formation, and as such is unconscious. Six of the 8 patients never returned to their former work. Three of them are still incapacitated because of their anxieties in relation to resuming their previous work, and the other 3 patients changed to another type of work. The 2 housewives succeeded in securing the help of their families in their housework after they had been trying unsuccessfully to do this for years prior to the injury. This resentful, dissatisfied attitude of patients toward their work can be found on careful psychiatric exploration immediately after injury, and the development of anxiety neuroses in such patients can be anticipated. At that stage patients with head injury give no evidence of anxiety related to the injury but the great majority exhibit a contemplative mood, actually expressing their intention of returning to work. Their initial physical disability protects them at this time from resuming their responsibilities. Therefore the duration of this "preneurotic interval" varies according to the severity of the physical injury. Roussy and Lhermitte [3] have described this phase, designating it as one of "incubation and contemplation." Final judgment about the patient's mental reaction to the injury can be made only after he is physically fit to return to work. This accounts for the frequent delay in onset of mental symptoms as compared with the time of onset of headaches and dizziness. The longest delay was observed by us in a 53 year old worker whose case has been mentioned in a previous part of this paper because of the occurrence of delayed nightmares. For many years he had had an inner conflict between his dislike of an occupation which he found monotonous and his feeling that it was his duty to stay on the job for the sake of financial security. For the six months following injury, while physically incapacitated because of a complicating fracture of the leg, he declared himself resolved to return to full work as soon as his leg was healed. His mood was pensive, given to meditation over his type of work, but not anxious. When he was faced with the necessity of resuming his occupation, however, typical anxiety states and nightmares developed, a condition which has made it impossible for him to resume full time work, and he is about to make a change in his occupation. This type of neurosis, originating in a conflict between a sense of duty or self respect and the patient's idea of self preservation, may well be designated a "conflict neurosis," as was done by Symonds [12] in a recent paper. He differentiated another type, "fear neurosis," which originates in the experience of frightening events which the patient is unable to balance and which initiate fear reactions. The great majority of neuroses which develop after civilian head injuries are "conflict neuroses," since the actual accident is usually of short duration and devoid of frightening content, and may be totally blotted out by long-lasting retrograde amnesia or preceding consumption of alcohol. In only 4 of our patients was the reaction that of a "fear neurosis." In them there was no delay in onset of anxiety, but they showed pronounced emotional disturbance while in the hospital, and their anxiety dreams occurred during the first nights in the hospital. One was a laborer aged 21 who had been dragged along by a car for a long distance before hitting the pavement. His anxiety neurosis started while in the hospital, and he gave the impression of suffering from a severe fright reaction. Nightmares, during which he relived the frightening experience, tormented him during the nights following the accident and for a few months thereafter.

No attempt was made to prevent the development of a "conflict neurosis" in civilians by early psychotherapy. It appears that if there is evi-

14. Schilder, P.: Neuroses Following Head and Brain Injuries, in Brock, S.: Injuries of the Skull, Brain and Spinal Cord, Baltimore, William Wood & Co., 1940.

dence of conflict in relation to pending obligations the "preneurotic interval" between the injury and full development of the neurosis is the most suitable time for preventive psychiatric measures.

Unless a post-traumatic neurosis developed, no post-traumatic change of attitude toward employment could be noted. Patients who had unsatisfactory work records continued after injury to be failures at work. In particular, it should be stressed that mere dissatisfaction with work does not imply the presence of a conflict, conducive to the development of post-traumatic neurosis. There were several patients who openly disliked their kind of work, for instance, students who hated school and planned to leave and start work, and several adult workmen. But, unlike the potential neurotic patient, they openly strove to bring about a change and often succeeded in doing so without having to resort to the detour of neurotic mechanisms originating from conflicts.

In addition, our 7 patients with personality changes which were evidently caused by damage to the brain did not show any changes of attitude toward employment. These observations suggest the advisability of careful scrutiny of underlying causes before the statement is made that injury to the brain is often associated with change of attitude toward work. To understand such a change, an accompanying statement about the presence or absence of post-traumatic neurosis is mandatory.

OTHER ENVIRONMENTAL COMPLICATIONS

A mechanism similar to that resulting from conflict in relation to occupation could be found in relation to other environmental problems. Problems of litigation and compensation were associated with an unfavorable psychiatric course in 20 of 34 patients who had such problems. All these patients had been harassed by debts and other financial obligations for some time before injury. After injury their interest centered around the problem of compensation, through the solution of which they hoped to be relieved of their previous anxieties.

For instance, 1 patient had been unable to pay dues on her insurance for almost a year prior to her injury. Another patient had been anticipating with anxiety the time when her brother was expected to enter the Army, and by a coincidence this happened a few days after her head injury. Two other patients had been overconscientious and overanxious in obtaining financial security. These were the patients who after injury centered their anxieties about the compensation problem, as though a satisfactory settlement of their claims might present an escape from their previous anxieties.

PSYCHOLOGIC REACTION TO THE INJURY ITSELF IN PATIENTS WHO DID NOT PRESENT POST-TRAUMATIC NEUROSES

The psychologic reaction to the injury itself was studied in detail in 35 patients who had not shown any post-traumatic mental symptoms. Of these, 18 showed no psychologic reaction whatever to the injury. Answers, such as "I never gave it a thought," or "It never bothered me," were given repeatedly. The remaining 17 patients showed a reaction which should not be confused with that of post-traumatic neurosis, since its course and prognosis differ considerably from the latter condition. These patients reported initial concern about either the outcome of their injury or their ability to go through conditions repeating the circumstances of the accident, but they were able to control their thoughts and to consider the problem with equanimity. For instance, patients who had had traffic accidents reported that they had first felt nervous when driving but that they drove just the same, only more carefully. People who had been struck by traffic reported that they looked around more carefully before crossing a street but that they crossed just the same. Patients who had been injured during football games decided to wear a helmet or not to play any more since they had to support their families and were anxious to avoid further work disability. Another patient who had been injured while roller skating decided to frequent a rink other than the one at which she had been injured, where better instruction was given and stricter discipline was maintained. A few patients were concerned about the physical outcome for a short while after injury. Some remembered things they had read about amnesia and thought they might forget much of their past; others worried about careless remarks which they had heard concerning the seriousness of their injury, but they were comforted after the first reassuring discussion with the physician. No one in this group had any prolonged work disability. The majority returned to work immediately after discharge from the hospital. None had any post-traumatic anxiety dreams. Thus, their reaction to the injury promoted attention, sharpened judgment and resulted in suitable measures toward self preservation. The pretraumatic, as well as the post-traumatic, adjustment to work and social obligations was undisturbed in this group. This fact and the absence of post-traumatic nightmares make it possible to forecast a favorable development of a condition which otherwise shows points

of similarity to the early stages of post-traumatic neurosis.

We estimated that of all patients with head injuries about one-third showed no psychologic reaction whatever to the injury; one-third showed apprehension resulting in a healthy adjustment and in increased measures for self preservation, while the other third reacted with the development of neurosis.

WORKING EFFICIENCY FOLLOWING INJURY IN RELATION TO PRETRAUMATIC AND POST-TRAUMATIC PSYCHIATRIC CONDITIONS

Of the 42 patients who returned to work within seven days, only 1 patient, a Negro woman, had any post-traumatic mental sequelae. Her pretraumatic alcoholism and hypochondriasis were somewhat worse after injury. Of the 71 patients returning to work within one month, the proportion with post-traumatic mental symptoms was also low, namely, 21 per cent. On the other hand, of the 60 patients whose working disability was longer than one month, the proportion with post-traumatic mental symptoms was high, namely, 65 per cent. All the 18 patients returning to work after four months had psychiatric complications. Two of the 18 patients, however, presented personality changes only, without psychogenic complications. Of the remaining 16 patients with post-traumatic neurosis, 15 had anxiety states and 1 an obsessive-compulsive condition. However, this patient who complained that after injury he had phobias and compulsions forcing him, for instance, to try over and over whether he had locked the door of his garage, was seen only once and refused to submit to further follow-up study.

These observations reveal that post-traumatic mental complications are the chief cause of long-lasting employment disability after civilian head injuries. These complications are predominantly composed of anxiety reactions.

SUMMARY AND CONCLUSIONS

Of a group of 200 patients, post-traumatic mental symptoms developed after head injury in 31.5 per cent. A number of extrinsic and intrinsic factors were examined in relation to the development of these symptoms. Pretraumatic factors having a high incidence of post-traumatic mental symptoms were advancing age, the married status in men, certain national stocks, certain occupations, the type of injury and, among the psychiatric disturbances, pretraumatic symptoms based on anxiety. Post-traumatic factors having a high incidence of post-traumatic mental symptoms were the initial occurrence of coma and post-traumatic amnesia, certain accompanying injuries, a prolonged stay in the hospital and the presence of headaches and dizziness. In particular, prolonged duration of headaches and dizziness was associated with a high incidence of mental symptoms. Other physical sequelae of the injury lasting more than six months had an equally high incidence of mental symptoms (73 per cent). Post-traumatic nightmares were regularly associated with additional symptoms of anxiety. In addition, certain environmental complications, occupational difficulties in particular, and problems of litigation and compensation were correlated with a high incidence of post-traumatic mental symptoms.

Of the patients with post-traumatic mental symptoms, the largest group, 48 patients, had post-traumatic anxiety states. Twenty-three of these patients had previously normal personalities, whereas the remainder had preexisting psychiatric liabilities. In all but 1 of these 48 patients the issue was complicated by environmental difficulties, such as occupation, litigation, etc.

The post-traumatic neuroses of all but 3 of the 26 previously normal patients conformed to the picture of anxiety neurosis. The psychiatric syndrome in patients with pretraumatic psychiatric complications varied through modification of the preexisting condition, although 19 of the 26 patients presented predominantly anxiety symptoms.

Whereas anxiety symptoms were the predominant mental features in the post-traumatic neuroses, particularly neuroses in previously normal patients, symptoms of personality change only, such as euphoria, moodiness and apathy, in addition to changes in the intellectual status, were presented by 7 patients with severe head injuries.

Mental symptoms, particularly symptoms of anxiety, are, with headaches and dizziness, the commonest symptoms in convalescence. They are also the most common symptoms relating to disability and are undoubtedly the major cause of disability, in particular of prolonged disability. A number of factors enter into the production of such anxiety symptoms, the most direct being reproduction of fears related to the injury and accentuation and elaboration of preexisting conflicts in relation to occupational and financial questions. The latter factor accounts for the delay in onset of mental symptoms observed in several patients until they had recovered physically and were again faced with their obligations.

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DELIRIUM

III. ELECTROENCEPHALOGRAPHIC CHANGES ASSOCIATED WITH ACUTE ALCOHOLIC INTOXICATION

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CINCINNATI

Previous studies of the electroencephalograms of patients with delirium have demonstrated a close correlation between changes in the electrical activity of the brain and the level of consciousness, but no correlation with the more personal aspects of behavior, such as the character or expression of anxiety, the nature of sense deceptions or the content of thought.[1] The earliest changes in the electroencephalogram consisted of a progressive decrease in the frequency to the 6 to 8 per second range. In cases of more severe delirium there were increasing irregularity, disruption of synchrony with the appearance of low voltage fast activity and, finally, development of much high voltage irregular, slow activity with a frequency of 2 to 6 cycles per second. The severity of the electroencephalographic changes was related to the intensity, duration and reversibility of the noxious factors involved and to the premorbid status of the central nervous system, but was more or less independent of the nature of the noxious agents. The electroencephalographic changes were found to be reversible to the extent to which the clinical delirium was reversible. This was true whether there was spontaneous recovery or whether certain physiologic or chemical derangements were specifically corrected, as by changes in posture, by administration of oxygen, dextrose, insulin or adrenal cortex extract or by blood transfusion.

The administration of alcohol is an easy means of producing an acute delirium which is rapidly reversible. This affords an opportunity for further study of the relation between the electroencephalogram and the level of awareness in an experimentally induced and readily reversible delirium.

Gibbs, Gibbs and Lennox [2] studied a patient in alcoholic coma and found high voltage slow waves. With recovery the record returned to normal. Davis and associates [3] studied the effects of alcohol on the electroencephalogram and on the level of consciousness in 6 normal men. They gave 2 cc. of 100 per cent alcohol (mixed with fruit juices and sugar) per kilogram of body weight over a period of one hour. Analysis of the electroencephalograms of 2 subjects by means of the Grass analyzer showed a reduction in energy on the fast side of the frequency spectrum, particularly in the range of 10 to 13 cycles per second with relatively low concentrations of alcohol. With higher concentrations episodes of slow waves (4 to 8 cycles per second) intruded into the subject's characteristic electroencephalographic pattern and appeared in the spectrum analysis as an increase of energy in the corresponding frequency band. The subject's performance on the psychometric tests was definitely impaired while the concentration of alcohol in the blood was at its height (125 to 140 mg. per hundred cubic centimeters) and for an hour thereafter, but returned approximately to normal in four or five hours. The alcohol level of the blood was still elevated (90 to 120 mg. per hundred cubic centimeters) and the modifications of the electroencephalogram were still prominent at the end of the experiment, but the subjects were fairly sober. Mirsky and associates [4] studied the electroencephalograms of 4 normal

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Major George L. Maltby, Medical Corps, Army of the United States, and Major I. Arthur Mirsky, Medical Corps, Army Air Forces, gave help in the initial formulation of this study.

1. Romano, J., and Engel, G. L.: Delirium: I. Electroencephalographic Data, Arch. Neurol. & Psychiat. **51**:356 (April) 1944. Engel, G. L., and Romano, J.: Delirium: II. Reversibility of the Electroencephalogram with Experimental Procedures, ibid. **51**:378 (April) 1944.

2. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Effects on the Electroencephalogram of Certain Drugs Which Influence Nervous Activity, Arch. Int. Med. **60**:154 (July) 1937.

3. Davis, P. A.; Gibbs, F. A.; Davis, H.; Jetter, W. W., and Trowbridge, L. S.: The Effects of Alcohol upon the Electroencephalogram (Brain Waves), Quart. J. Stud. on Alcohol **1**:626, 1941.

4. Mirsky, I. A.; Piker, P.; Rosenbaum, M., and Lederer, H.: Adaptation of the Central Nervous System to Various Concentrations of Alcohol in the Blood, Quart. J. Stud. on Alcohol **2**:35, 1941.

rabbits in which alcohol was injected intravenously. When the animals became intoxicated and comatose, diminution in amplitude and frequency of all cortical waves occurred. Occasionally large slow waves appeared. With clinical recovery the electroencephalogram returned to normal, in spite of the fact that the alcohol concentration of the blood remained unchanged.

METHODS AND MATERIALS

Seven normal subjects and 4 patients with chronic alcoholism who had occasional convulsions associated with drinking bouts were utilized for this study. One of the latter subjects was studied twice. Three of the normal subjects were given 1 Gm. of alcohol per kilogram of body weight (50 per cent solution sweetened with saccharin) followed in about eighty minutes by 0.5 Gm. of alcohol per kilogram of body weight. Four

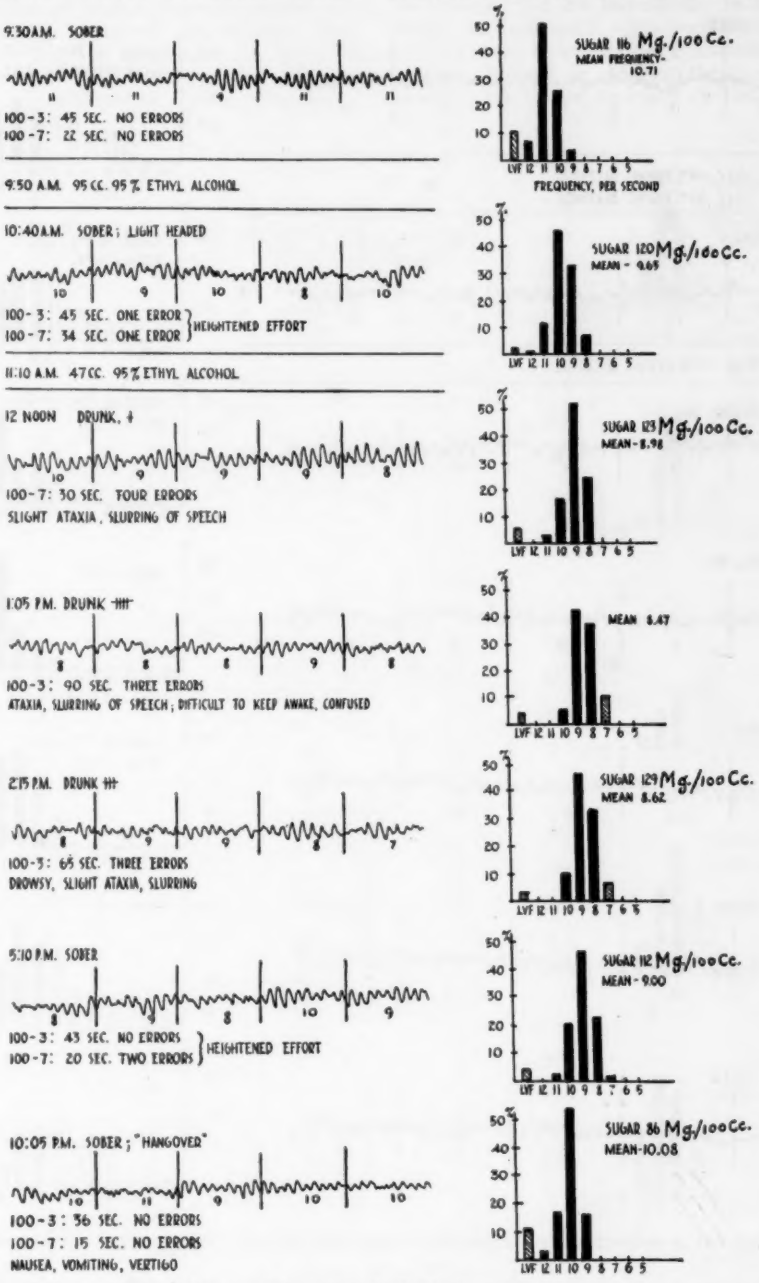
9:30 A.M. SOBER
100-3: 45 SEC. NO ERRORS
100-7: 22 SEC. NO ERRORS
SUGAR 116 Mg./100 Cc.
MEAN FREQUENCY-10.71
9:50 A.M. 95 CC. 95% ETHYL ALCOHOL
10:40 A.M. SOBER; LIGHT HEADED
100-3: 45 SEC. ONE ERROR
100-7: 34 SEC. ONE ERROR
HEIGHTENED EFFORT
SUGAR 120 Mg./100 Cc.
MEAN - 9.65
11:10 A.M. 47 CC. 95% ETHYL ALCOHOL
12 NOON DRUNK, +
100-7: 30 SEC. FOUR ERRORS
SLIGHT ATAXIA, SLURRING OF SPEECH
SUGAR 123 Mg./100 Cc.
MEAN-8.98
1:05 P.M. DRUNK +++
100-3: 90 SEC. THREE ERRORS
ATAXIA, SLURRING OF SPEECH; DIFFICULT TO KEEP AWAKE, CONFUSED
MEAN 8.47
2:15 P.M. DRUNK +++
100-3: 65 SEC. THREE ERRORS
DROWSY, SLIGHT ATAXIA, SLURRING
SUGAR 129 Mg./100 Cc.
MEAN 8.62
5:10 P.M. SOBER
100-3: 43 SEC. NO ERRORS
100-7: 20 SEC. TWO ERRORS
HEIGHTENED EFFORT
SUGAR 112 Mg./100 Cc.
MEAN - 9.00
10:05 P.M. SOBER; "HANGOVER"
100-3: 36 SEC. NO ERRORS
100-7: 15 SEC. NO ERRORS
NAUSEA, VOMITING, VERTIGO
SUGAR 86 Mg./100 Cc.
MEAN-10.08
FREQUENCY, PER SECOND

Fig. 1.—Tracings for a normal subject with acute alcoholic intoxication.

The control electroencephalogram shows high alpha activity, with a mean frequency of 10.71 waves per second. At the time of maximum intoxication (1:05 p. m.) the mean frequency had slowed to 8.47 waves per second, with 11 per cent of 7 per second activity. At 5:10 p. m. the subject was sober but still made errors when tested. The final record (10:05 p. m.), taken during a severe "hang-over," showed a mean frequency of 10.8 waves per second. The blood sugar level was 30 mg. lower than the morning control level.

normal subjects were given only the first dose and observed for only one hour. The subjects with chronic alcoholism received, in addition, a third dose of 0.5 Gm. of alcohol per kilogram of body weight between one hundred and one hundred and twenty minutes after the first dose. The alcohol was administered orally, after an overnight fast, and each dose was consumed within two to fifteen minutes. With the exceptions already noted, observations were carried out over the course of seven to twenty-five hours.

All signs and symptoms were noted, and the diagnosis was made in accordance with the criteria set down by Jetter [5] as essential for the determination of clinical intoxication. The subject was considered clinically intoxicated (+++ to ++++) when there were

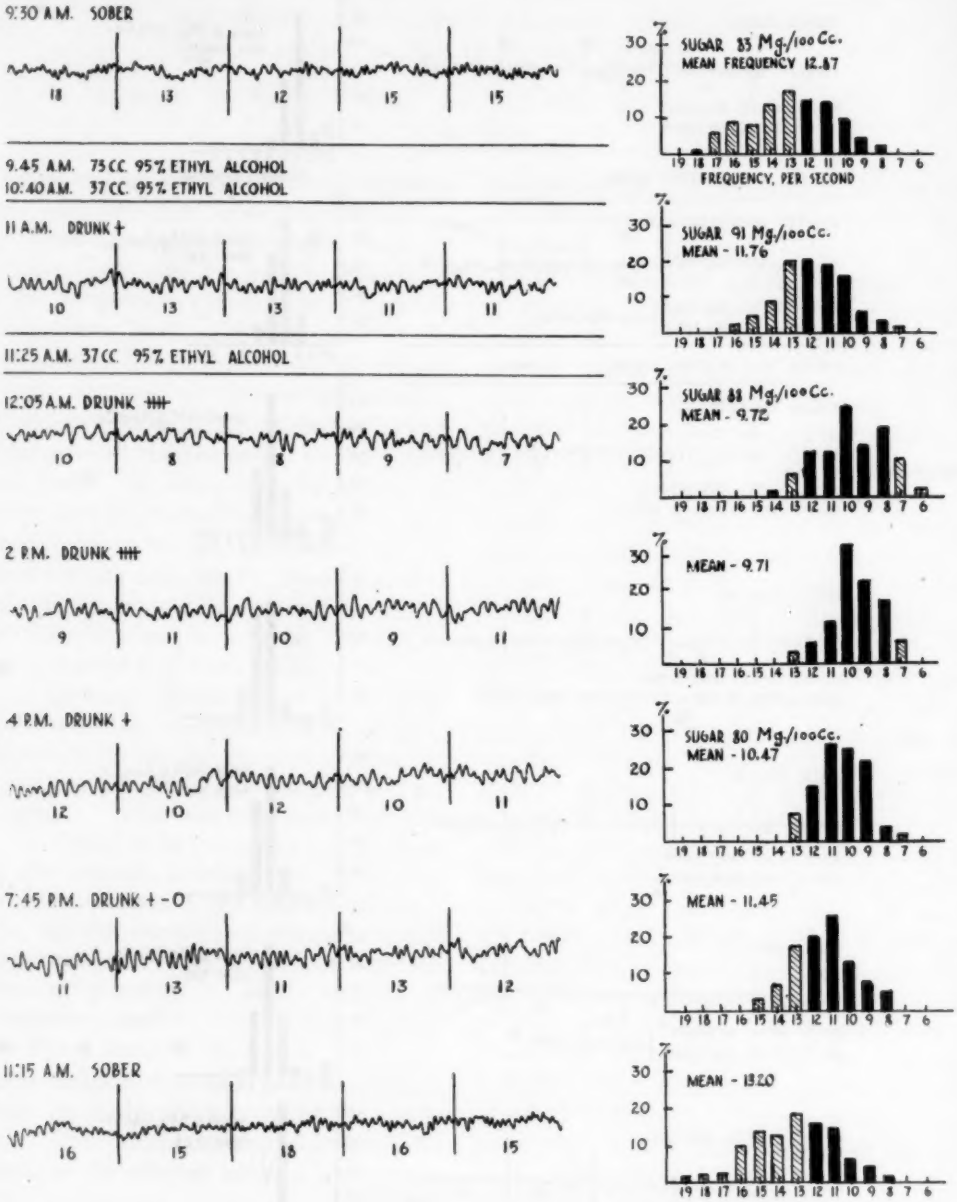
9:30 A.M. SOBER
18 13 12 15 15
9:45 A.M. 75 CC. 95% ETHYL ALCOHOL
10:40 A.M. 37 CC. 95% ETHYL ALCOHOL
11 A.M. DRUNK +
10 13 13 11 11
11:25 A.M. 37 CC. 95% ETHYL ALCOHOL
12:05 A.M. DRUNK +++
10 8 8 9 7
2 P.M. DRUNK +++
9 11 10 9 11
4 P.M. DRUNK +
12 10 12 10 11
7:45 P.M. DRUNK + - 0
11 13 11 13 12
11:15 A.M. SOBER
16 15 18 16 15
SUGAR 83 Mg./100 Cc.
MEAN FREQUENCY 12.87
FREQUENCY, PER SECOND
SUGAR 91 Mg./100 Cc.
MEAN - 11.76
SUGAR 88 Mg./100 Cc.
MEAN - 9.72
MEAN - 9.71
SUGAR 80 Mg./100 Cc.
MEAN - 10.47
MEAN - 11.45
MEAN - 13.20

Fig. 2.—Tracings for a subject with chronic alcoholism and associated convulsions, taken during acute intoxication.

The control electroencephalogram reveals a dominant fast record (10 to 14 waves per second) with faster (15 to 18 waves per second) and slower (8 to 9 per second) activity. There were infrequent individual waves with a frequency of 6 to 7 per second which do not appear in the spectrum as such because they were added with faster waves to make the totals for each one second interval. With maximum intoxication the mean frequency shifted from 12.87 to 9.71 waves per second; twenty-five and a half hours after the first dose of alcohol, the record had returned to the control state.

5. Jetter, W. W.: Studies in Alcohol: Diagnosis of Acute Alcoholic Intoxication by Correlation of Clinical and Chemical Findings, Am. J. M. Sc. **196**:475, 1935.

abnormality of gait, ataxia, abnormality of speech, various emotional changes and gross fluctuations in the level of awareness. When the subject reported the first subjective effects of alcohol, it was recorded as 1 to 2 plus (+ to ++), the grade depending on the intensity of the symptoms, although at this stage the subject was not considered grossly intoxicated. In addition, more detailed psychologic tests to determine the level of awareness were carried out on the normal subjects. These included tests of orientation, handwriting, serial subtraction, digit span and interpretation of proverbs.

The electroencephalograph was a standard three channel, ink-writing oscillograph, constructed by Mr. Albert Grass. For the subjects with chronic alcoholism six electrodes were placed over the frontal, parietal and occipital regions on the two sides, and routine monopolar and bipolar tracings were taken to rule out the presence of focal abnormalities. For the normal subjects only bipolar fronto-occipital tracings were taken. Electroencephalograms were recorded before alcohol was given and at various intervals up to twenty-five hours after administration of the first dose of alcohol. Gross changes in the electroencephalogram were sought for by inspection. In addition, the spectrums of frequency distribution in fronto-occipital tracings were obtained by a quantitative method.[6] This method consisted in counting the number of waves per second interval for a record of two hundred seconds.

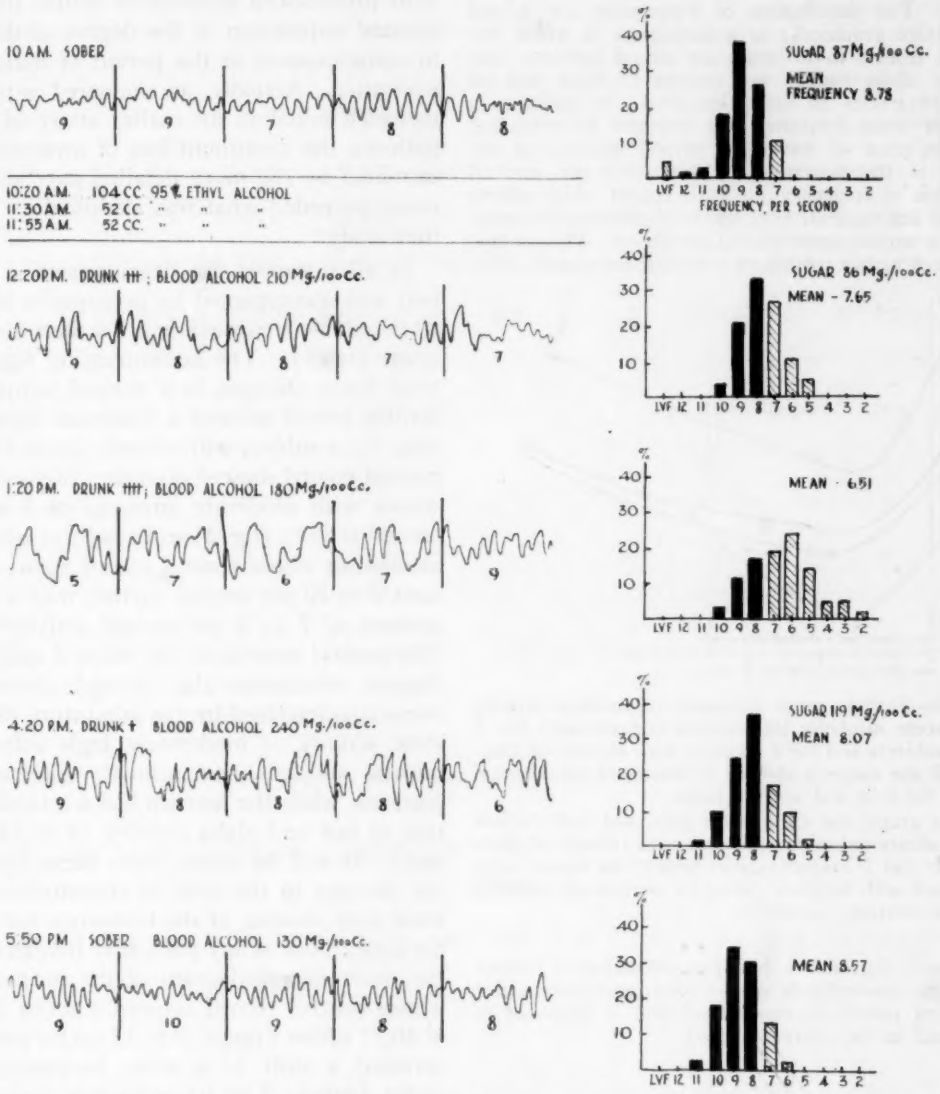
10 A.M. SOBER
9 9 7 8 8
10:20 A.M. 104 CC. 95% ETHYL ALCOHOL
11:30 A.M. 52 CC. " " "
11:55 A.M. 52 CC. " " "
12:20 P.M. DRUNK III ; BLOOD ALCOHOL 210 Mg./100 Cc.
9 8 8 7 7
1:20 P.M. DRUNK IIII; BLOOD ALCOHOL 180 Mg./100 Cc.
5 7 6 7 9
4:20 P.M. DRUNK I BLOOD ALCOHOL 240 Mg./100 Cc.
9 8 8 8 6
5:50 P.M. SOBER BLOOD ALCOHOL 130 Mg./100 Cc.
9 10 9 8 8
%
40
30
20
10
LVF 12 11 10 9 8 7 6 5 4 3 2
FREQUENCY, PER SECOND
SUGAR 87 Mg./100 Cc.
MEAN FREQUENCY 8.78
SUGAR 86 Mg./100 Cc.
MEAN - 7.65
MEAN - 6.51
SUGAR 119 Mg./100 Cc.
MEAN 8.07
MEAN 8.57

Fig. 3.—Tracings for a subject with chronic alcoholism and associated convulsions, taken during acute intoxication.

The control electroencephalogram reveals a mean frequency of 8.78 waves per second, with some slower frequencies appearing paroxysmally. With maximum intoxication slow frequencies became prominent, and the mean frequency was reduced to 6.51 waves per second.

6. Engel, G. L.; Romano, J.; Ferris, E. B., Jr.; Webb, J. P., and Stevens, C. D.: A Simple Method of Determining Frequency Spectrums in the Electroencephalogram: Observations on Effects of Physiologic Variations in Dextrose, Oxygen, Posture, and Acid-Base Balance on the Normal Electroencephalogram, Arch. Neurol. & Psychiat. **51**:134 (Feb.) 1944.

The distribution of waves per second was then expressed as percentages of the whole, i. e., the percentages of second intervals containing 10 waves, 9 waves, 8 waves, etc. When waves faster than 12 per second were of very low voltage (less than 5 microvolts), they were all grouped together as "low voltage fast" activity. The fast waves of higher voltage were counted. Only the dominant waves that returned completely, or almost completely, to the base line were counted, the superimposed frequencies of low voltage being ignored. This method of counting is illustrated in the accompanying figures. The distribution of frequencies per second is expressed graphically as a nomogram, in which frequencies from 8 to 12 cycles per second inclusive (the so-called alpha range) are charted in black and all other frequencies in cross hatching. In addition, a value for mean frequency was obtained by averaging the distribution of waves per second interval, as expressed in the nomogram. This yields an over-all expression of frequency for each record which allows for rapid and accurate comparison of shifts in frequency under the various experimental conditions. This method has proved highly reliable in detecting even small shifts

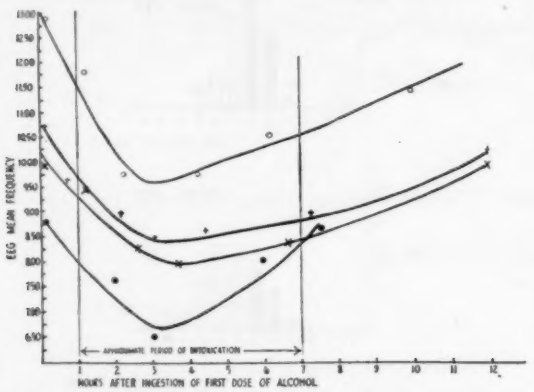

Fig. 4.—Shift in mean frequency of cerebral activity during acute alcoholic intoxication and recovery for 2 normal subjects and for 2 subjects with chronic alcoholism. All the subjects showed evidences of intoxication between the first and seventh hour.

In this graph, the curve with solid and with hollow circles indicate values for subjects with chronic alcoholism (Huc and P respectively in table); the curves with crosses and with daggers, values for normal subjects (R and S respectively in table).

in frequency distribution during manipulation of various physiologic determinants of the electroencephalogram [6] and during pathologic conditions [1] and is discussed in more detail in the references cited.

RESULTS

The development of acute intoxication followed the familiar course. The first subjective symptoms were noted by the normal subjects within forty minutes, while the subjects with chronic alcoholism generally did not acknowledge any symptoms until well into the second hour, usually after receiving the second dose of alcohol. In addition to the classic symptoms of intoxication already described, all subjects showed pronounced somnolence, from which, however, they could always be aroused. The electroencephalogram taken during this sleep did not differ from the pattern obtained during normal sleep. For the purposes of this study we kept the subjects as alert as possible during the electroencephalographic recordings by interrupting the run at frequent intervals, by talking, ringing a bell and having the subject open the eyes; no records made during sleep were included in this study. This pronounced somnolence results in an exaggerated impression of the degree of disturbance in consciousness at the period of maximum intoxication. Actually, as compared with the disturbance noted in an earlier study of delirious patients, the maximum loss of awareness as determined by the more detailed psychologic tests never exceeded what was classified as "mild" in that study.[1]

In all instances the development of intoxication was accompanied by progressive slowing of all countable frequencies in the electroencephalogram (table). The accompanying figures illustrate these changes in a normal subject whose control record showed a dominant alpha pattern (fig. 1), a subject with chronic alcoholism whose control record showed dominant high voltage fast waves with moderate amounts of 8 to 12 per second activity (fig. 2) and a subject with chronic alcoholism whose control record showed a dominant 9 to 10 per second rhythm with a moderate amount of 7 to 8 per second activity (fig. 3). The control records of the other 2 subjects with chronic alcoholism also showed abnormal patterns characterized by the admixture of fast and slow activity of moderately high voltage. Six normal subjects had normal, dominant alpha patterns, while the seventh had a mixed distribution of fast and alpha activity (8 to 15 per second). It will be noted from these figures that the changes in the level of consciousness correlated with slowing of the frequency but not with the appearance of any particular frequency. Thus, the electroencephalogram of the normal subject whose control record showed a mean frequency of 10.71 cycles (range, 9 to 12 cycles per second) revealed a shift to a mean frequency of 8.47 cycles (range, 7 to 10 cycles per second), with only 11 per cent of 7 per second waves at the height of intoxication. The record during maximum intoxication still falls within the range of accepted normality but represents a profound shift in frequency for this subject. This shift in frequency is far beyond any range previously established during alterations within physiologic zones induced by administration of dextrose and oxygen or by changes in posture for 10 normal subjects.[6] Identical results were obtained for the other normal subjects (table). Similarly, the

Changes in Electroencephalographic Frequencies During Acute Alcoholic Intoxication

Subject	Experiment	Time, Min.	Blood Sugar, Mg./100 Cc.	Electroencephalographic Frequency Spectrums, Percentage of Waves per Second																			Mean Frequency per Sec.	Degree of Intoxication †
				LVF*	19	18	17	16	15	14	13	12	11	10	9	8	7	6	5	4	3	2		
R. (Normal male)	Control	0	116	11	..	..	..	..	..	..	..	8	51	26	4	..	..	..	..	..	..	..	10.71	Sober
	95 cc. 95% ethyl alcohol	45	120	2	..	..	..	..	..	..	..	1	11	46	33	7	..	..	..	..	..	..	9.65	±
	47 cc. 95% ethyl alcohol	130	123	6	..	..	..	..	..	..	..	..	3	16	51	24	..	..	..	..	..	..	8.98	+
		185	...	4	..	..	..	..	..	..	..	..	..	6	42	37	11	..	..	..	..	..	8.47	++++
		265	129	3	..	..	..	..	..	..	..	..	..	10	47	33	7	..	..	..	..	..	8.62	+++
		440	112	4	..	..	..	..	..	..	..	..	3	21	47	23	2	..	..	..	..	..	9.00	Sober
		720	86	10	..	..	..	..	..	..	..	3	17	54	16	..	..	..	..	..	..	..	10.08	Sober, hang-over
S. (Normal male)	Control	0	91	8	..	..	..	..	..	..	..	..	21	46	22	3	..	..	..	..	..	..	9.92	Sober
	100 cc. 95% ethyl alcohol	70	103	1	..	..	..	..	..	..	..	..	6	45	38	10	..	..	..	..	..	..	9.47	±
	50 cc. 95% ethyl alcohol	160	123	..	..	..	..	..	..	..	..	..	..	4	35	44	17	..	..	..	..	..	8.26	++++
		225	109	2	..	..	..	..	..	..	..	..	..	3	23	46	22	4	..	..	..	..	7.99	++++
		410	111	1	..	..	..	..	..	..	..	..	..	4	35	51	9	..	..	..	..	..	8.34	++
		720	99	5	..	..	..	..	..	..	..	..	19	49	24	3	..	..	..	..	..	..	9.88	Sober
W. (Normal male)	Control	0	100	3	..	..	..	..	1	2	6	12	22	30	21	3	..	..	..	..	..	..	10.52	Sober
	95 cc. 95% ethyl alcohol	30	125	..	..	..	..	..	..	..	2	4	14	29	36	15	1	..	..	..	..	..	9.60	+
	47 cc. 95% ethyl alcohol	90	105	..	..	..	..	..	..	..	..	2	10	26	36	22	4	..	..	..	..	..	9.21	++
		165	105	1	..	..	..	..	..	..	..	2	8	15	45	24	6	..	..	..	..	..	9.01	++
		390	80	4	..	..	..	..	..	..	2	8	20	32	25	8	..	..	..	..	..	..	10.00	Sober
Re. (Normal male)	Control	0	105	9	..	..	..	..	..	..	..	11	51	24	5	..	..	..	..	..	..	..	10.75	Sober
	100 cc. 95% ethyl alcohol	45	90	5	..	..	..	..	..	..	..	3	14	58	18	2	..	..	..	..	..	..	9.98	+
B. (Normal male)	Control	0	115	..	..	..	..	..	..	..	..	5	55	39	1	..	..	..	..	..	..	..	10.64	Sober
	100 cc. 95% ethyl alcohol	50	110	..	..	..	..	..	..	..	..	..	2	44	47	7	..	..	..	..	..	..	9.41	+
Sp. (Normal male)	Control	0	100	..	..	..	..	..	..	..	..	..	..	7	69	24	..	..	..	..	..	..	8.83	Sober
	100 cc. 95% ethyl alcohol	55	110	..	..	..	..	..	..	..	..	..	..	2	39	48	11	..	..	..	..	..	8.32	±
H. (Normal male)	Control	0	105	5	..	..	..	..	..	..	..	..	1	26	55	13	..	..	..	..	..	..	9.16	Sober
	100 cc. 95% ethyl alcohol	50	105	5	..	..	..	..	..	..	..	..	..	4	30	48	13	..	..	..	..	..	8.26	+
P. (Chronic alcoholic addict)	Control	0	83	..	..	1	6	9	8	14	17	15	14	10	4	2	..	..	..	..	..	..	12.87	Sober
	110 cc. 95% ethyl alcohol	75	91	..	..	..	..	2	5	9	20	20	19	16	6	3	1	..	..	..	..	..	11.76	+
	51 cc. 95% ethyl alcohol	135	88	..	..	..	..	..	..	1	6	12	12	25	14	19	10	1	..	..	..	..	9.72	++++
		255	..	..	..	..	..	..	..	..	3	6	12	34	23	17	6	..	..	..	..	..	9.71	++++
		375	80	..	..	..	..	..	..	..	7	15	27	25	22	3	1	..	..	..	..	..	10.47	+
		600	..	..	..	..	..	..	3	7	18	20	26	13	8	5	..	..	..	..	..	..	11.45	±
		1,530	..	..	1	2	2	10	12	13	19	16	15	6	4	1	..	..	..	..	..	..	13.06	Sober
Huc. (Chronic alcoholic addict)	Control	0	87	5	..	..	..	..	..	..	..	1	2	18	38	26	10	..	..	..	..	..	8.78	Sober
	208 cc. 95% ethyl alcohol	120	86	..	..	..	..	..	..	..	..	..	..	4	21	33	26	11	5	..	..	..	7.65	+++
		180	..	..	..	..	..	..	..	..	..	..	..	3	11	17	19	24	14	5	5	2	6.51	++++
		360	119	..	..	..	..	..	..	..	..	..	1	10	24	37	17	10	1	..	..	..	8.07	+
		450	...	..	..	..	..	..	..	..	..	..	2	18	33	31	14	2	..	..	..	..	8.57	Sober

* LVF indicates low voltage fast activity.
† The degree of intoxication is graded on the basis of 1 to 4 (+ to ++++).

tracing for the subject with chronic alcoholism whose control records showed a mean frequency of 12.87 cycles (range, 8 to 18 cycles per second) showed a shift in mean frequency to 9.71 cycles (range, 7 to 13 cycles per second) at the height of intoxication (fig. 2). During the period of developing intoxication and during recovery this patient's record actually showed a higher percentage of frequencies within the so-called normal range (8 to 12 waves per second) than did his control record. This case, again, illustrates the importance of the degree of shift in frequencies rather than the absolute frequency obtained. Finally, the electroencephalogram of the subject whose control records showed dominantly slow activity (mean frequency, 8.78 cycles; range, 7 to 11 cycles per second) yielded much more slow activity (fig. 3) at the height of intoxication (mean frequency, 6.51 cycles; range, 2 to 10 cycles per second). Expressed in terms of change in mean frequency, gross intoxication was associated with a decrease in mean frequency of 2 to 3 cycles per second, regardless of the initial pattern.

The correlation between the changes in the electroencephalogram and the signs of "gross intoxication" (+++ and ++++) was good, although during the phase of recovery, when the patients described themselves as sober, the electroencephalogram had not yet returned to the control base line. However, more careful psychologic tests for the level of awareness in 3 of the normal subjects revealed minor defects at this time. With essentially similar electroencephalograms during induction of and recovery from intoxication, the performance of the subject, both subjectively and objectively, was consistently better during recovery. The reason for this discrepancy is not fully understood, but it is possible that it is more dependent on psychologic than on physiologic factors.

In the case of the subject who had a severe "hang-over," characterized by headache, vertigo on movement of the head, nausea and vomiting, the electroencephalogram had returned almost to the control pattern at the height of the "hang-over."

COMMENT

These data confirm essentially the previous observation that the earliest change of the electroencephalogram during delirium consists of a general decrease in frequency, with a shift of frequency distribution spectrums to the slower range.[1] As with the delirious patients, these early changes were not associated with any striking change in regularity. In the present studies, however, we had the advantage of knowing the character of the predelirium electroencephalogram. With this information, it is now possible to state that in correlation of the effects of noxious substances on the electroencephalogram and on the level of consciousness, the degree of change in frequency is of more significance than the appearance of any particular frequency. Indeed, with initial records that are predominantly fast, the tracing obtained during mild disturbances in consciousness may actually appear more normal than the control record. These results, again, emphasize the need for caution in the interpretation of single electroencephalograms for patients with disturbances in consciousness due to changes in cerebral metabolism.

The question whether alcohol increases the convulsive tendency, as represented in the electroencephalogram, cannot be answered by these preliminary observations on the 4 alcoholic patients with convulsions. The shift toward slow frequencies included not only the dominant elements, whether they were fast or slow, but the more paroxysmal rhythms.

SUMMARY

Acute alcoholic intoxication was induced in 7 normal subjects with normal electroencephalograms and in 4 subjects with chronic alcoholism who had occasional convulsions associated with drinking bouts and whose control electroencephalograms showed abnormally fast or slow activity. The distribution of frequencies was determined, and, in addition, the mean frequency was calculated. In all instances the development of intoxication was accompanied by progressive slowing of the brain waves, but the degree of slowing proved a more reliable index than the development of any particular wave frequency. Expressed in terms of mean frequency, gross intoxication was associated with a change in mean frequency of 2 to 3 cycles per second. When the preintoxication record was fast or fast normal, the record obtained during gross intoxication had a frequency distribution within the normal range (8 to 12 waves per second) and contained no frequencies below 7 waves per second. Indeed, some abnormally fast records became more "normal" during intoxication. With recovery the electroencephalogram returned to the preinduction status. A close correlation was demonstrated between the electroencephalogram and the level of consciousness, but not with the more personal aspects of behavior.

Cincinnati General Hospital.

ACTION OF BARBITURATES ON THE CEREBRAL CORTEX

ELECTROENCEPHALOGRAPHIC STUDIES

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BOSTON

The work of Quastel and associates [1] has shown that narcotics even in low concentrations inhibit specifically the oxidation in vitro by brain cells of d-glucose, lactic acid and pyruvic acid. This inhibitory action takes place, not by preventing the access of oxygen to brain cells nor by interfering with the activation of oxygen by brain catalysts, but by impairing the hydrogen-liberating mechanisms (dehydrogenase activity) which normally result in activation of lactic or pyruvic acid.

Narcotics inhibit this dehydrogenase activity, presumably by forming surface films or adsorption compounds which prevent the access of hydrogen donators to their activating enzymes.[2] Thus, the effect of the narcotic is to diminish the ability of the brain cells to oxidize lactic or pyruvic acid or d-glucose. The access of oxygen to the cell is quite unimpaired, but the diminished oxidizing ability of the cells results in a lowering of the amount of energy available for these cells to accomplish their functional activities. This depression of the normal functional activity of the cells in question results in, or is, "narcosis."

The chain of oxidative processes in brain cells may be represented in outline by the following simplification: At the beginning of the chain the principal substrate is d-glucose, which, through a long chain of intermediary changes, is finally oxidized to carbon dioxide and water, with liberation of large amounts of energy. One of the chief intermediary stages in the first part of the breakdown of d-glucose is the oxidation of lactic acid to pyruvic acid. Meyerhof [3] showed the dependence of this stage on the presence of a coenzyme which acts as a specific carrier linking lactic dehydrogenase with lactic acid in such a way that the dehydrogenase can remove hydrogen from the lactic acid, with the production of pyruvic acid. The dehydrogenase which activates lactic acid as a hydrogen donator is highly specific [4] and is present in greater quantities in brain than in muscle.[5]

It is this stage of dehydrogenase activity which is inhibited by narcotics of the barbiturate type. To repeat, these narcotics do not interfere with the catalytic activation of oxygen, or with the access of oxygen to the brain cells, but inhibit the activity of the dehydrogenase stages of pyruvic and lactic acid catabolism.

The mechanism of this dehydrogenase activity may well be, as Quastel and Wooldridge [6] suggested, a polarization of the molecule of the substrate by an electric field at the cell surface to which the molecule is attached. If the polarization is sufficient, the molecule will receive its critical energy of activation and will then be able to function as a hydrogen donator.

This chain of events in the cell respiration of brain tissue has been worked out from data gained from in vitro experiments with minced fresh brain and with brain slices, variations of the Barcroft and Warburg technics [7] being used for the most part. To extend these studies to the respiration of brain cells in vivo necessitates some other technic. Electroencephalography may well furnish pertinent data in this field.

From the Department of Neuropsychiatry, Harvard Medical School, and the Psychiatric Department and Electroencephalographic Laboratory, Massachusetts General Hospital.

1. Quastel, J. H., and Wheatley, A. H. M.: Narcosis and Oxidation of Brain, Proc. Roy. Soc., London, s.B **112**:60-79, 1932. Davis, D. R., and Quastel, J. H.: Dehydrogenations by Brain Tissue: Effects of Narcotics, Biochem. J. **26**:1672-1684, 1932. Quastel, J. H.: Respiration in the Central Nervous System, Physiol. Rev. **19**:135-183, 1939.

2. Sen, K. C.: The Effect of Narcotics on Some Dehydrogenases, Biochem. J. **25**:849-857, 1931.

3. Meyerhof, O.: Ueber die Atmung der Froschmuskulatur, Arch. f. d. ges. Physiol. **175**:20-87, 1919.

4. The dehydrogenase which activates lactic acid has been isolated, and its chemical constitution is known (Schlenk, F.: Whither Enzyme Chemistry, Texas Rep. Biol. & Med. **2**:183-205, 1944).

5. Green, D. E., and Brosteaux, D.: Lactic Dehydrogenase of Animal Tissues, Biochem. J. **30**:1489-1508, 1936.

6. Quastel, J. H., and Wooldridge, W. R.: Some Properties of Dehydrogenating Enzymes of Bacteria, Biochem. J. **22**:689-702, 1928.

7. Dixon, M.: Manometric Methods, London, Cambridge University Press, 1934.

The work of Hoagland [8] demonstrated clearly the influence of changes in brain cell respiration on the frequency rates of cortical potentials. It is probable that cortical cells build up potential gradients in the process of their respiratory metabolism, and, as Hadidian and Hoagland [8c] stated:

> These may be of the nature of diffusion potentials across cell membranes which possess definite electrical impedance and which discharge when the potentials reach a critical value. In such a system the discharge frequency depends on the speed with which the metabolic factor can load the capacities of the cell walls to their critical discharge potentials. The absolute frequency would thus depend on the rate of cellular respiration and on the electrical impedance of the cell walls.

The purpose of the present study was to determine whether the electroencephalogram of the intact human being would give any evidence with regard to impairment by barbiturates of cortical cell respiration or of the impedance characteristics of the cell membranes.

METHOD

Electroencephalograms were recorded by the standard method, which is too well known to need repetition here. Standard placement of six scalp electrodes was used, one electrode being placed on each frontal, parietal and occipital region. Dextrose (d-glucose) (50 Gm.) was given by mouth to every subject to insure adequate amounts of initial substrate.

A base line electroencephalogram was made with a Grass six channel ink-writing oscillograph (the heart rate being recorded on one channel), and the recording was continued through intravenous injection of the barbiturate and for approximataely one hour after its administration.

Three drugs were used: sodium amytal, sodium pentothal and sodium pentobarbital, the doses of sodium amytal varying from 0.25 to 0.65 Gm. and the doses of sodium pentothal from 0.125 to 0.5 Gm. The dose of sodium pentobarbital used was 0.3 Gm.

RESULTS

The initial effect of slow intravenous injection of any of the three drugs was completely consistent and dramatic. It was characterized by the appearance of high voltage fast activity, which is defined here as a frequency of 21 to 32 cycles per second,[9] and of voltages certainly above 25 microvolts, and frequently reaching 100 microvolts. Fast frequencies resulting from injection of sodium amytal were described by Cohn and Katzenelbogen [10] and by Rubin, Malamud and Hope.[11] Electrical activity of the kind just described was observed in every subject to whom

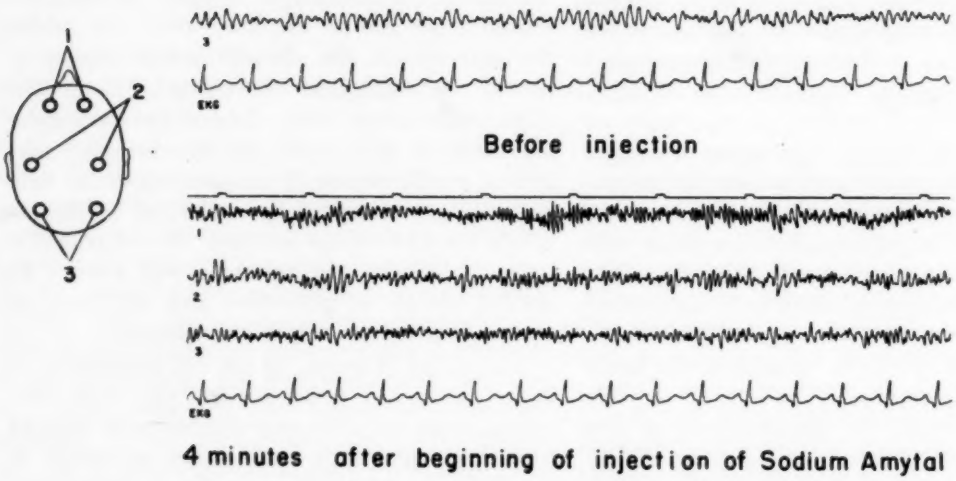

Fig. 1.—Effect of sodium amytal on the electroencephalogram.

8. (*a*) Hoagland, H.: Chemical Pacemakers and Physiological Rhythms, in Alexander, J.: Colloid Chemistry, New York, Reinhold Publishing Corporation, 1944, vol. 5; (*b*) Pacemakers of Human Brain Waves in Normals and in General Paretics, Am. J. Physiol. **116**:604-615, 1936. (*c*) Hadidian, Z., and Hoagland, H.: Chemical Pacemakers: I. Catalytic Brain Iron; II. Activation Energies of Chemical Pacemakers, J. Gen. Physiol. **23**:81-99, 1939.

9. These figures are the extremes of the range of frequencies observed. The most commonly occurring rate was 25 to 26 cycles per second.

10. Cohn, R., and Katzenelbogen, S.: Electroencephalographic Changes Induced by Intravenous Sodium Amytal, Proc. Soc. Exper. Biol. & Med. **49**:560-563, 1942.

11. Rubin, M. A.; Malamud, W., and Hope, J. M.: Electroencephalogram and Psychopathological Manifestations in Schizophrenia as Influenced by Drugs, Psychosom. Med. **4**:355-361, 1942.

these drugs were given. Sodium amytal was given to 16 patients (twenty experiments); sodium pentothal to 22 patients (50 experiments), and sodium pentobarbital to 2 patients (two experiments). The subjects were patients from the psychiatric wards of the Massachusetts General Hospital with psychoneuroses of various kinds. There were 18 males and 16 females, with an age range of from 14 to 59 years.

In figure 1 is shown the type of electrical activity characteristic of the effect of slow administration of small doses of these drugs. In the upper record are bipolar tracings from the frontal, parietal and occipital regions respectively taken before administration of sodium amytal. In the lower record, taken four minutes after the beginning of the injection, the same leads are

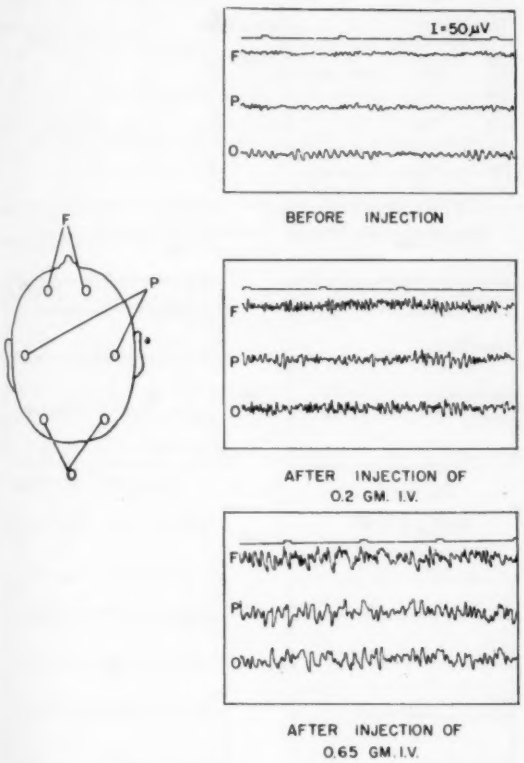

Fig. 2.—Effect of intravenous injection of sodium amytal on the electroencephalogram.

represented; here high voltage fast activity is present in every lead. The procedure employed in slow administration of the drug was to take two minutes in giving the first grain (0.065 Gm.) of the drug and from that point to administer 1 grain (0.065 Gm.) per minute. Thus, this tracing of the action of the drug four minutes after the beginning of the injection represents the effect of the injection of 3 grains (0.195 Gm.) of sodium amytal.

When a larger dose of sodium amytal was given, a second effect was seen in the electroencephalogram. This consisted of slowing of the frequencies until delta waves of 3 to 4 per second developed (see fig. 2). These were not waves characteristic of sleep and were present while the patient was still responsive.

Sodium pentothal when injected intravenously produced a similar effect. When the dose was small high voltage fast activity dominated the record, but when the dose was increased delta waves appeared.

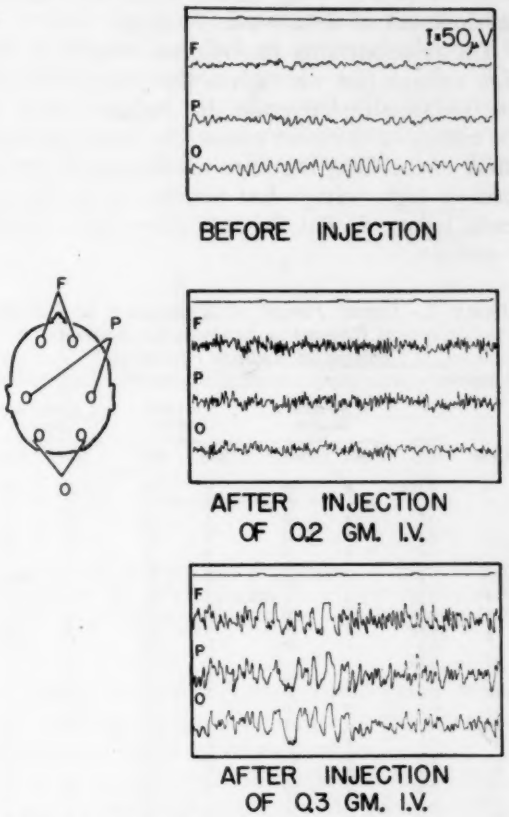

Fig. 3.—Effect of intravenous injection of sodium pentothal on the electroencephalogram.

It thus appears that barbiturates may have two distinct effects on the electroencephalogram: one, the production of high voltage fast activity by low concentrations of the drug, and the other, slowing of the frequencies when the concentration is increased. This concept of a dual effect receives support from the observation that swift administration of sodium pentothal, as in the induction of surgical anesthesia (0.2 Gm. in ten seconds), produces delta activity within one minute of the start of injection. Barbiturates are known to be rapidly destroyed in the body, so that the period of high concentration is necessarily brief.

The development of high voltage fast activity as the initial result of slow intravenous injection of these two barbiturates occurred in every subject to whom they were given, without exception. The same effect was also observed in 2 subjects who received sodium pentobarbital (0.3 Gm.) intravenously.

The development of 25 per second waves in the brain potentials of cats under anesthesia induced with pentobarbital was reported by Derbyshire and his co-workers.[12] With anesthetic doses of this drug Hoagland and associates[13] demonstrated slowing of the alpha rhythm and development of delta waves in dogs.

The most striking observation relating to the high voltage fast waves was their appearance in the electroencephalogram in various parts of the cortex at different times. In every case the effect of the drug began to manifest itself in the form of high voltage fast activity in the frontal leads before it did in any other lead (tables 1 and 2).

TABLE 1.—*Latent Period of Response* in Various Cortical Regions to Intravenous Administration of Sodium Pentothal*

Case	Dose, Gm.	Frontal Region Min.	Frontal Region Sec.	Parietal Region Min.	Parietal Region Sec.	Occipital Region Min.	Occipital Region Sec.
1	0.125	0	45	2	15	2	15
2	0.2	1	30	3	0	3	30
3	0.2	4	30	4	45	5	0
4	0.2	1	0	1	30	1	30
5	0.2	3	0	4	0	9	0
6	0.2 + 0.4	1	10	1	20	3	..
		0	50	1	20	3	20
7	0.25	3	0 (50 μV)	3	30	5	30
8	0.25	1	20	1	20	1	30
9	0.25 + 0.5	7	30	8	00	11	00
		1	10	5	00	7	00
10	0.25	..	..†	3	00	4	00
11	0.3	1	40	2	0	2	40
12	0.3	0	30	1	30	3	0
13	0.3	3	0	4	30	4	15
14	0.3	0	30	0	45	6	00
15	0.3	3	00	3	20	3	40
16	0.3	1	30	2	30	4	0
17	0.3	1	0	2	00	3	30
18	0.35	2	30	3	30	4	30
19	0.5	0	45	1	15	4	0
20	0.5	0	45	3	0	8	0
21	0.5	1	30	2	00	3	00
22	0.5	..	..†	0	45	1	00

* The arbitrary criterion of response used in this table, and in table 2, is the first appearance after the beginning of the injection of three consecutive waves each of which is above 25 microvolts.
† Not measurable because of muscle movement.

In fig. 4, the normal base line record is shown first, and the second tracing is that taken one minute after the beginning of the injection, i. e., after 0.25 Gm. of sodium pentothal had been injected. The frontal leads already show pronounced change, and three minutes after the beginning of the injection the change has appeared in the parietal leads; but not until seven minutes after the beginning of the injection, that is, when 0.3 Gm. had been administered, did the change appear in the occipital leads. This striking progression of the effect from the frontal lobes through the parietal to the occipital region was observed in every subject to whom these barbiturates were given.

TABLE 2.—*Latent Period of Response in Various Cortical Regions to Intravenous Injection of Sodium Amytal*

Case	Dose, Gm.	Frontal Region Min.	Frontal Region Sec.	Parietal Region Min.	Parietal Region Sec.	Occipital Region Min.	Occipital Region Sec.
1	0.25	5	20	6	0	No high voltage fast activity	
2	0.35	2	15	3	0	4	15
3	0.35	..	..*	3	20	4	0
4	0.35	Not recorded		3	0	Did not reach 25 μV	
5	0.45	5	0	6	30	13	30
6	0.5	2	0	5	0	Did not reach 25 μV	
7	0.5	5	0	6	0	6	20
8	0.5	5	0	5	30	6	0
9	0.5	6	20	7	0	9	30
10	0.5	6	0	7	10	7	50
11	0.5	6	30 (50 μV)	9	0	Did not reach 25 μV	
12	0.5	4	20 (15 μV)	5	0	6	20
13	0.5	Not recorded		2	10	5	30
14	0.6	4	0	5	0	7	0
15	0.65	..	..*	3	30	6	30
16	0.65	2	0	10	0	Did not reach 25 μV	
17	0.65	3	30	4	30	6	0
18	0.65	3	0	4	0	..	..
19	0.85	5	30	7	0	9	0

* Not measurable because of muscle movement.

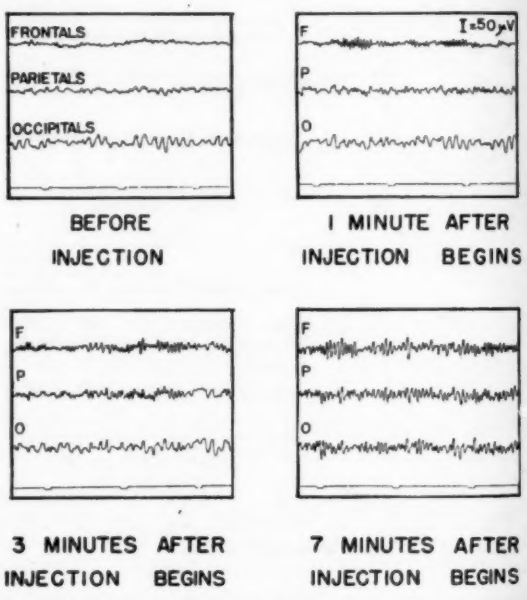

Fig. 4.—Progression of the effects of sodium pentothal in various cortical regions.

12. Derbyshire, A. J.; Rempel, B.; Forbes, A., and Lambert, E. F.: Effect of Anesthetics on Action Potentials in Cerebral Cortex of the Cat, Am. J. Physiol. **116**:577-596, 1936.

13. Hoagland, H.; Himwich, H. E.; Campbell, E.; Fazekas, J. F., and Hadidian, Z.: Effects of Hypoglycemia and Pentobarbital Sodium on Electrical Activity of Cerebral Cortex and Hypothalamus (Dogs), J. Neurophysiol. **2**:276-288, 1939.

Moreover, when the patient was allowed to recover from the effect of the drug, the regression of the effect was in the opposite direction, i. e., the occipital region recovered first, followed by the parietal areas, whereas in the frontal lobes the effect lingered for a long time.

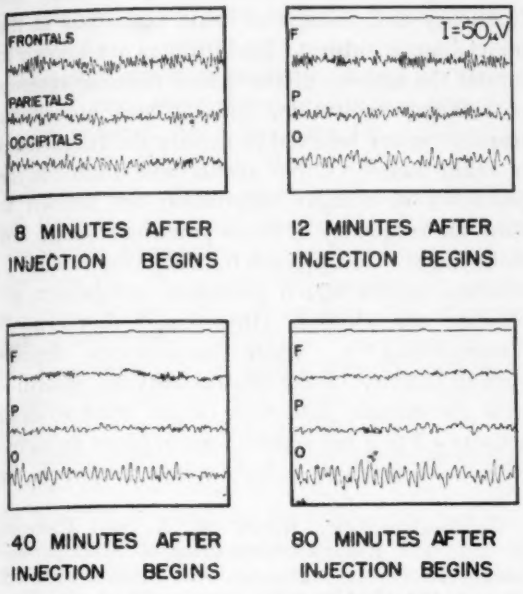

Fig. 5.—Stages in recovery from the effect of intravenous injection of 0.5 Gm. of sodium pentothal.

In the subject whose record is shown in figure 5, the occipital regions were free of high voltage fast activity within twelve minutes of the injection, but it took eighty minutes to clear the frontal lobes.

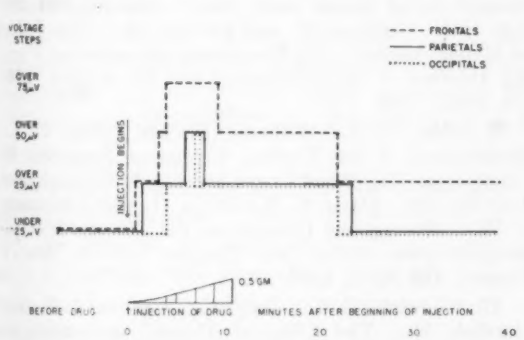

Fig. 6.—Progression and regression of high voltage fast activity in different regions of the cortex after intravenous injection of 0.5 Gm. of sodium pentothal.

In figure 6 this progression and regression of effect has been charted, and from this graph one other observation can be made. The change in the electroencephalogram from the frontal lobes not only precedes that from the other regions of the cortex but is of greater magnitude. In this graph the time relations are plotted for the development of each of three steps in the rise in voltage. The moment, timed from the beginning of the injection, at which the voltage first reaches 25 microvolts is plotted, and then the times for 50 and 75 microvolts respectively. In charting the progress of recovery, the last moment at which voltages as high as 75 microvolts were recorded is plotted; then the drop from 50 microvolts and, finally, the drop from 25 microvolts. For the subject whose record is shown in this figure, the only region of the cortex to reach voltages as high as 75 microvolts was the frontal, and forty minutes later the tracing from the frontal lead had not returned completely to the base line wave pattern.

The same effect was observed with the intravenous administration of sodium amytal, as can be seen in figure 7. Although with this drug

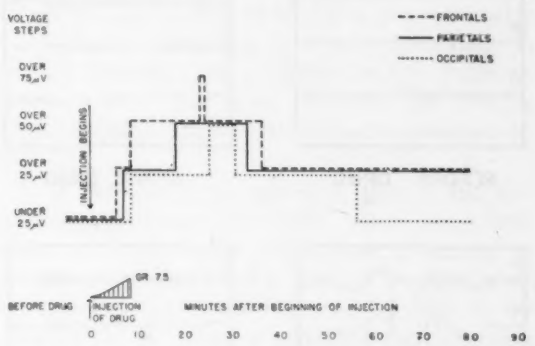

Fig. 7.—Progression and regression of high voltage fast activity in different regions of the cortex after intravenous injection of 7.5 grains (0.45 Gm.) of sodium amytal.

the change in the electroencephalogram lasted rather longer, the preponderance of the effect on the frontal lobes is again evident.

It thus appears that these barbiturates—sodium amytal and sodium pentothal—have an effect on the electroencephalogram which is most pronounced in the regions of the cortex which are of most recent ontogenetic and phylogenetic development. Salmon [14] showed that pentobarbital has less narcotic effect on young animals in which the cortical layers are not yet fully developed than on adult animals. The progression from one region of the cortex to another is too slow to be explained by differences in cerebral circulation.

Three patients were given sodium amytal by mouth in doses of 9 grains (0.585 Gm.); the electroencephalogram of 1 patient showed no effect; the second patient went to sleep and his

14. Salmon, T. N.: The Effect on the Growth Rate of Thyro-Parathyroidectomy in Newborn Rats, Endocrinology **23**:446-457, 1938.

electroencephalogram showed normal sleep waves but no other effects; the third patient's record showed all the effects observed with intravenous injection, but with a longer latent period from the time the drug was taken. High voltage fast activity appeared first in the frontal leads twenty-two minutes after the capsules were taken and reached the occipital areas in thirty-one minutes. This effect was maximal in one hour and forty-six minutes, after which delta waves appeared. There are obviously wide individual differences in reaction to the drug. At the height of the action of the drug, in the doses indicated, its effect is preponderant, and even though the patient is unconscious, the electroencephalographic record may show only high voltage fast activity. At a later stage, when the patient goes to sleep

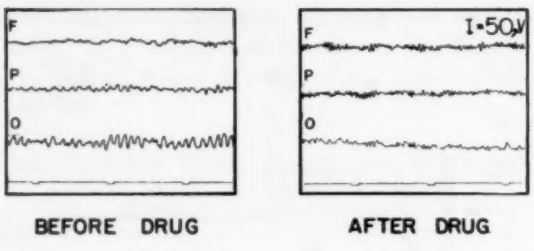

Fig. 8.—Sleep and arousal under medication with sodium pentothal.

under the influence of one of these drugs, the electroencephalogram may change from the abnormal pattern characteristic of administration of barbiturates to a normal sleep pattern (fig. 8). At this depth of sleep there is no difference between the electroencephalogram taken with the patient under the influence of the drug and that which is taken during normal sleep. But when the patient is roused from this drugged sleep, the electroencephalogram does not return to its normal pattern but shows the high voltage fast activity typical of the drug.

COMMENT

In the introduction to this paper the reasons for the design of these experiments were outlined, the essential purpose being, as stated in the final paragraph, to use the electroencephalogram in elucidation of the action of barbiturates on the respiration and on the membrane permeability of the cortical cells.

The results obtained show that the barbiturates—sodium amytal, sodium pentothal and sodium pentobarbital—influence profoundly the frequency and voltage of brain potentials in the intact human subject. Barbiturates are known to inhibit the activity of the dehydrogenase systems of cellular respiration, and changes in cellular respiration are believed to modify the frequencies of brain waves. Other agents which impede the processes of cellular respiration are known to slow the frequency of brain potentials (e. g., low blood sugar,[15] low oxygen tension,[16] cretinism [17]), whereas agents which stimulate metabolism accelerate the rhythm (thyroxin,[18] diathermy,[16] dinitrophenol [19]). These barbiturates—depressors of activity of the central nervous system—slow the electric potentials of the brain to delta activity (3 to 4 per second) when given in such a way as to produce a high concentration in the

15. Hoagland, H.; Rubin, M. A., and Cameron, D. E.: The Electroencephalogram of Schizophrenics During Insulin Hypoglycemia and Recovery, Am. J. Physiol. **120**:559-570, 1937. Brazier, M. A. B.; Finesinger, J. E., and Schwab, R. S.: Characteristics of the Normal Electroencephalogram: II. The Effect of Varying Blood Sugar Levels on the Occipital Cortical Potentials in Adults During Quiet Breathing, J. Clin. Investigation **23**:313-317, 1944. Himwich, H. E., and others: Clinical, Electroencephalographic, and Biochemical Changes During Insulin Hypoglycemia, Proc. Soc. Exper. Biol. & Med. **40**:401-402, 1939. Davis, P. A.: Effect on the Electroencephalogram of Alterations of Blood Sugar Level, Am. J. Physiol. **133**:259-260, 1941. Gellhorn, E., and Kessler, M.: The Effect of Hypoglycemia on the Electroencephalogram at Varying Degrees of Oxygenation of the Blood, ibid. **136**: 1-6, 1942.

16. Gibbs, F. A.; Williams, D., and Gibbs, E. L.: Modification of the Cortical Frequency Spectrum by Changes in CO_2, Blood Sugar and O_2, J. Neurophysiol. **3**:49-58, 1940. Davis, P. A.; Davis, H., and Thompson, J. W.: Progressive Changes in the Human Electroencephalogram Under Low Oxygen Tension, Am. J. Physiol. **123**:51-52, 1938.

17. Himwich, H. E.; Daly, C.; Fazekas, J. F., and Herrlich, H.: The Effect of Thyroid Medication on Brain Metabolism of Cretins, Am. J. Psychiat. **98**: 489-493, 1942.

18. Ross, D. A., and Schwab, R. S.: The Cortical Alpha Rhythm in Thyroid Disorders, Endocrinology **25**:75-79, 1939. Rubin, M. A.; Cohen, L., and Hoagland, H.: The Effect of Artificially Raised Metabolic Rate on the Electroencephalogram of Schizophrenic Patients, ibid. **21**:536-540, 1937. Himwich and others.[17]

19. Hoagland, H.; Rubin, M. A., and Cameron, D. E.: Brain Wave Frequencies and Cellular Metabolism: Effects of Dinitrophenol, J. Neurophysiol. **2**:170-172, 1939.

brain, but the initial, and more striking, effect is the breaking of high voltage fast activity into the record, not as an acceleration of the original frequency, but as a new rhythm already established at a frequency higher than 20 cycles per second. In other words, there is no gradation through the intermediate frequencies between the normal alpha rate and the ultimate fast activity.

This suggests that two effects may be taking place; if one is interference with the dehydrogenase systems, the other may be a change in permeability of the cell membrane.

The cortical cells are separated from each other and from the substrate-bearing blood supply by semipermeable membranes; it is at these surface interfaces that the enzyme mechanisms previously outlined operate—it is here that the dehydrogenase becomes "activated," i. e., changes its electronic structure in such a way that electrons become available for the oxidation of the substrate. In fact, this transfer of electrons is the fundamental mechanism, which in popular speech is called the "liberation of energy." It is actually the transfer of electrons by steps, from the system of more negative potential to the system of more positive potential until finally molecular oxygen is reached.[20]

When the metabolic oxidations in the brain are regarded from this basic electronic viewpoint, the importance of the characteristics of the surface interfaces becomes obvious.

It has long been known that narcotics decrease the permeability of cell membranes; Lillie,[21] in 1912, concluded that they caused an alteration in the surface membrane, and hence in the intracellular respiration, since reactions inside the cell are governed by the surface conditions. This conclusion has since been amply confirmed by Gellhorn and Weidling,[22] by Winterstein [23] and others.

Not only does the change in total permeability of the cell affect the internal chemical processes, but the changes in differential permeability are also influential. For example, a relatively greater increase in permeability for lactic acid with a relatively smaller increase in permeability for oxygen would result in an increase in the ratio of glycolysis to total oxidation in a cell.[24]

No change in cell permeability of this magnitude is likely without a resultant effect on the electroencephalogram, since however dependent the frequency of brain waves may be on chemical velocity within the cells, the ultimate rate of oscillation will also be governed by the impedance characteristics of the cell membrane.

It is likely that there may be two effects at work—one, the depressant effect of barbiturates on the dehydrogenase mechanisms, and the other, their effect on the dielectric of the cell membrane.

Elucidation of the relative importance of these two factors might be obtained from experiments designed to by-pass in some way one of these effects. Such a series of experiments, based on the substitution for dextrose of a substrate the dehydrogenase system of which is not vulnerable to barbiturate poisoning, is now in operation. A suitable substrate is available in the form of succinic acid; this acid, too, has its specific dehydrogenase, but its activity is not inhibited by narcotics.

It is reasonable to speculate that if the frequencies of brain potentials were dependent solely on intracellular respiration, it should be possible to maintain the rate of oscillation of these waves at the normal level in spite of the presence of barbiturates provided the cells were supplied with sufficient substrate in the form of succinate. If the resistance and capacity of the dielectric composing the cell wall were the preponderant factor in narcosis, it would be improbable that the frequencies of brain waves could be maintained at normal rates even by substrates invulnerable to barbiturates.[25] This

20. Barron, E. S. G.: Mechanisms of Carbohydrate Metabolism, in Nord, F. F., and Werkman, C. H.: Advances in Enzymology, New York, Interscience Publishers, Inc., 1943, vol. 3, pp. 149-189.

21. Lillie, R. S.: Antagonism Between Salts and Anesthetics, Am. J. Physiol. **29**:372-397, 1911-1912.

22. Gellhorn, E., and Weidling, K.: Beiträge zur allgemeinen Zellphysiologie, Arch. f. d. ges. Physiol. **210**:492-513, 1925.

23. Winterstein, H.: Die Narkose, Berlin, Julius Springer, 1926.

24. Rashevsky, N., and Landahl, H. D.: Permeability of Cells: Its Nature and Measurement from the Point of View of Mathematical Biophysics, in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L. I., New York, The Biological Laboratory, 1940, vol. 8, pp. 9-16.

25. In discussing our results, Hoagland (in a personal communication) suggested an alternative possibility to account for the appearance of high voltage fast rhythms despite probable over-all slowing of cortical respiration. He suggested that the fast rhythms may be due to the accumulation in the cells of lactate, since the barbiturates block its oxidation. Such an accumulation would raise the internal acidity of the cells. He expressed the opinion that the relation between cell respiration and frequency of brain wave rhythms is normally mediated by production of carbon dioxide, and he pointed out that the internal p_H of the cortical cells may determine their frequency of discharge, as it may in the respiratory center. Accumulation of lactic acid resulting from blockage of oxidation of lactate might lower the intracellular p_H and raise the frequency of the discharge.

problem is the subject of an investigation at present being carried out.

SUMMARY

In this study the electroencephalogram has been used in an attempt to elucidate the mechanics of cortical cell respiration in vivo.

One of the barbiturates—sodium amytal (in twenty experiments), sodium pentothal (in fifty experiments) and sodium pentobarbital (in two experiments)—was given intravenously to 32 patients.

For every subject to whom the barbiturate was given the electroencephalogram showed the development of high voltage fast activity.

In the patients who received larger doses per kilogram of body weight a second effect developed; this consisted of slow delta waves (3 to 4 per second).

In every subject the high voltage fast activity appeared first in the frontal leads, then in the parietal leads and finally in the occipital leads, and it disappeared in the reverse order. In other words, the regions of the cortex which are the most recent in phylogenetic development are most vulnerable to the action of barbiturates, as evidenced by the electroencephalogram.

In the first few minutes of injection, at the stage of maximal action of the drug, the patient may be unconscious without the appearance of any of the brain waves typical of sleep. At a later stage the patient may sleep deeply under the influence of the drug, at which time the electroencephalogram may show typical waves for normal sleep, but on the patient's arousal it will revert to the high voltage fast activity specific for the barbiturate.

ENCEPHALITIS ASSOCIATED WITH HERPES ZOSTER

REPORT OF A CASE

SIGMUND KRUMHOLZ, M.D., AND JOSEPH A. LUHAN, M.D.
CHICAGO

This case is reported because the literature contains few records of cases of encephalitis complicating herpes zoster in which the brain was examined histologically after death.

REPORT OF CASE

History.—Mrs. L. V., a housewife aged 58, white, was seen by one of us (S. K.) in consultation on April 6, 1942, because she had become restless, noisy and irrational. She had been in relatively good health except for occasional headaches and backache, for which she was taking acetylsalicylic acid. On March 7 neuralgic pain developed in the left side of the face and neck. Two days later examination by the family physician revealed a herpetic rash over the lower part of the face, the neck and the upper part of the shoulder and chest on the left side. The patient had a slight fever (temperature 99.5 to 100.0 F.), for several days. The vesicles disappeared in about fourteen days, but the pain persisted. On April 4 she complained of restlessness and insomnia. The next day she became irrational and noisy. On that day Dr. Maurice Oppenheim, a dermatologist, was called in consultation and concurred in the diagnosis of herpes zoster, expressing the conviction that the patient now presented a cerebral ailment. Nothing in the history relative to previous diseases and habits had any apparent bearing on the present illness.

Physical Examination.—Examination on April 6 by one of us (S. K.) revealed that the patient was well preserved. She was lying in bed and presented marked clouding of consciousness, accompanied by extreme restlessness. She did not respond to psychic stimuli, such as requests to protrude the tongue; she moaned, tossed about on the bed incessantly and reached out with her arms aimlessly into space. She was obviously out of contact with her environment but was not somnolent. There was pigmentation of the skin, involving the left side of the neck, the shoulder and the uppermost part of the chest, as well as the submental region and the lower portion of the face adjacent to the ear, an area representing the second, third and fourth cervical dermatomes. The rectal temperature on the morning of examination was 104.6 F.; the pulse was regular, with a rate of 120, and the respiratory rate was 34 per minute. The cardiac outline was within normal limits, and the heart presented no adventitious sounds. Except for bronchial rales the lungs were normal. The abdomen was not tender. The spleen and liver were not palpable. The blood pressure was 125 systolic and 80 diastolic.

Neurologic Examination.—The pupils were small and equal and reacted to light. The patient could not cooperate in tests of ocular motion, but no strabismus or nystagmus was observed. The corneal reflex was present on both sides. There was no facial paralysis, nor was there any masking or rigidity of facial expression or rigidity of the trunk and extremities, such as one sees in paralysis agitans. It was impossible to determine whether the patient had any weakness of the soft palate or of the swallowing musculature. The tongue lay in the midline. The fundi could not be seen. There was no discernible paralysis of the extremities or detectable muscle spasm on passive movements. The biceps and triceps reflexes were graded 2 plus; the patellar and achilles jerks were diminished. No pathologic reflexes were noted. There was withdrawal of the extremities and face to painful stimuli. Deep pressure on the calves of the legs produced withdrawal of the lower extremities. There was no significant nuchal rigidity. Kernig and Brudzinski signs were absent.

Laboratory Data.—The white blood cells on April 6 numbered 8,200 per cubic millimeter, of which 70 per cent were neutrophils, 29 per cent lymphocytes and 1 per cent large mononuclears. The erythrocyte count was 4,500,000 per cubic millimeter, and the hemoglobin concentration was 88 per cent (Tallqvist). A catheterized specimen of urine obtained on that day revealed no albumin or sugar, but the sediment contained a small number of granular casts and pus cells. Culture of a specimen of blood taken the same day revealed no growth when examined on April 13. The Kahn reaction of the blood was negative. The nonprotein nitrogen was 38.4 mg. per hundred cubic centimeters.

Spinal puncture performed later in the day revealed a cell count of 40 per cubic millimeter, of which 80 per cent were lymphocytes and 20 per cent polymorphonuclear leukocytes. The Pandy reaction of the spinal fluid was 1 plus; the Lange curve, 1110000000, and the dextrose content, 111 mg. per hundred cubic centimeters. (On the previous day the patient had received 1,500 cc. of a 5 per cent solution of dextrose, given intravenously.) The Wassermann reaction with 1 cc. of spinal fluid was negative.

Diagnosis.—It was the impression of the examiner that the patient had nonsuppurative encephalitis, although the possibility of a toxic psychosis was to be considered. In view of the relative absence of objective neurologic signs of a cerebral lesion, the diagnosis of encephalitis was reluctantly made. However, the acute nature of the disease, with high temperature, the presence of 40 cells per cubic millimeter in the spinal fluid at the receding stage of the herpes zoster, the absence of signs of infectious disease of the visceral organs and the lack of evidence incriminating any metabolic or exogenous toxic agent made the diagnosis of encepha-

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Read at a meeting of the Chicago Neurological Society, Oct. 15, 1942. An abstract of this paper, with discussion was published in the April 1943 issue of the ARCHIVES, page 633.

litis plausible. It is well known that neither encephalitis nor toxic encephalopathy produce a uniform clinical picture; the former, especially in the early stage, may show no objective focal neurologic signs, and the latter may at the onset present focal signs of cerebral disease.

Further Clinical Course.—The patient continued to be noisy and restless and moaned almost incessantly. On April 8, 9 and 10 she had periods of loud screaming. Involuntary urination occurred on April 9 and continued until her death. The nurses' records show that from time to time she was able to swallow sips of water and small quantities of liquid food. On April 6 sulfadiazine therapy was begun, which was discontinued on April 9, when the level of the drug in the blood was reported to be 3.1 mg. per hundred cubic centimeters. The rectal temperature remained in the vicinity of 102 F., rising above 104 F. two days before she died and reaching an agonal value of 108.6 F. The respiratory rate stayed rather constantly at about 30 per minute except on the last three days of her illness, when it rose to and remained over 40 to 50 per minute, the curve reflecting perhaps the development of bronchopneumonia. The patient died on April 15.

Gross Pathologic Study.—Necropsy was performed nine hours after death by Dr. Benjamin Neiman, who made the following anatomic diagnosis on the basis of the macroscopic observations: (1) fibrinous pericardosis; (2) pronounced parenchymatous degeneration of the myocardium; (3) bronchopneumonia involving the right lung; (4) fatty changes in the liver; (5) arteriosclerotic cysts of the kidneys; (6) fibrous adhesions of both pleural cavities, and (7) nodular goiter.

The fresh brain weighed 1,150 Gm. The leptomeninges were notably injected. The convolutions appeared somewhat flattened, and the leptomeninges were less transparent than normal. The lateral ventricles were of average width, and their lining was smooth.

We regret that the spinal cord, the ganglia of the posterior spinal roots and the gasserian ganglia were not obtained.

Microscopic Examination.—Examination of numerous sections from many blocks from all lobes of the brain, the subcortical white matter, the basal ganglia and the hypothalamus, stained with cresyl violet and with hematoxylin and eosin and by Weil's method for myelin sheaths, revealed no significant perivascular infiltrations in the meninges or the brain tissue and no demyelination. There were moderate edema and hyperemia of the leptomeninges of the convexities (fig. 1). Over the prefrontal convexities there was proliferation of arachnoid cells in the edematous meninges; small numbers of scavenger cells containing blood pigment were present, and deposition of hemosiderin within the cells of the first two cortical layers had occurred. There were conspicuous shrinkage spaces about the cortical ganglion cells, and in most of the cortical sections the larger ganglion cells showed powdery dissolution of Nissl substance and a

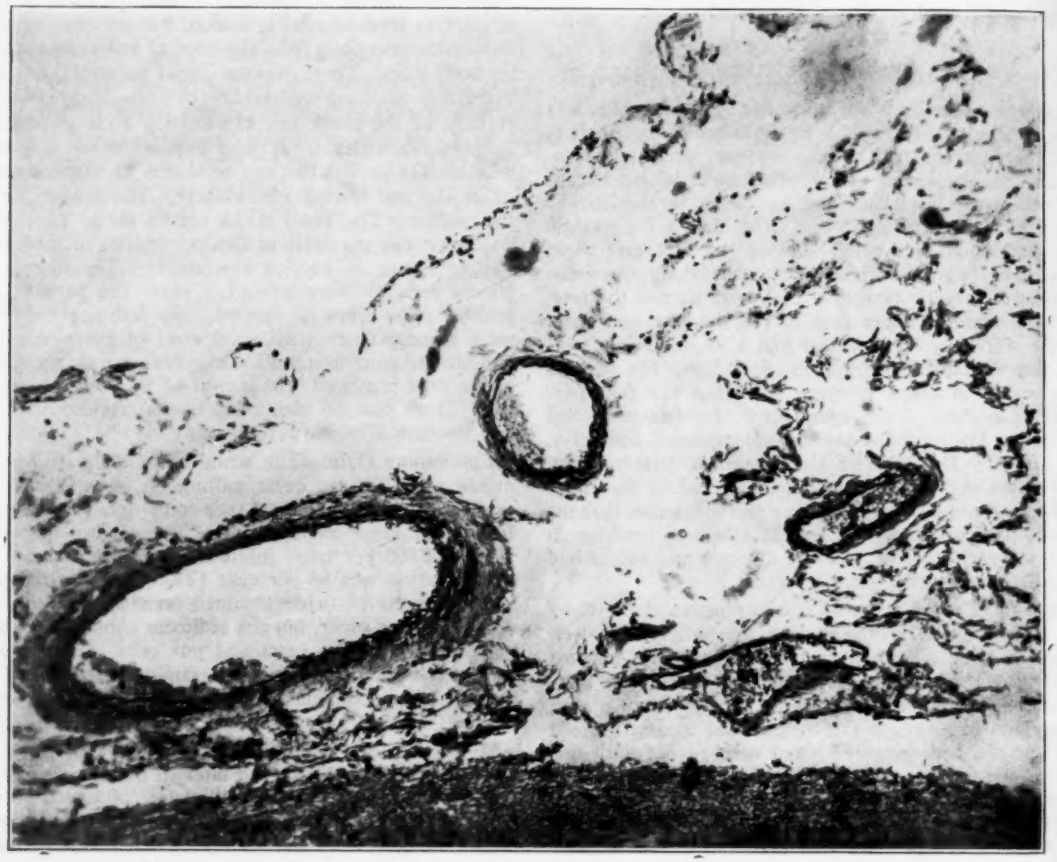


Fig. 1.—Section from right parietal region, showing edema of the surface leptomeninges. Hematoxylin and eosin stain.

picture resembling that of "acute ganglion cell disease" (fig. 2). In some cortical areas, especially the parietal, there was slight glial hyperplasia, especially of the satellite cells. Throughout the cortical sections the capillary bed was conspicuous, often with swelling of the endothelium. The white matter underlying the ependymal surfaces of the ventricles was distinctly hydropic. The basal ganglia and the hypothalamus revealed no signs of a proliferative type of encephalitis.

Similarly, the midbrain, the pons (including the entering fifth nerve trunk) and the cerebellum were free from any infiltrative changes.

Fig. 2.—Section of right parietal cortex, revealing picture of "acute ganglion cell disease" in the larger pyramidal cells, slight glial hyperplasia and prominent capillaries. Cresyl violet stain.

The medulla oblongata, however, presented unmistakable evidence of mild encephalitis, or meningoencephalitis, most pronounced at the midolivary level. There were occasional perivascular infiltrations in the leptomeninges and loose small round cell infiltrations, the latter occurring near the ventromedian surface of the medulla. The neural parenchyma contained infrequent round cell infiltrations within the adventitial (perivascular) spaces (figs. 3 and 4), near the olives, in the lateral reticular formation and the restiform bodies; in the caudal portion of the medulla these infiltrations were limited to the region of the cuneate fasciculus of one side. Scattered minute foci were noted on the other side, where small demyelinated areas lay adjacent to the olive. These tissue foci (figs. 5 and 6) revealed conspicuous glial proliferation, with the development of predominantly microglial forms, as shown by their polyblastic and rod-shaped nuclear structure. Occasional lymphocytes adjacent to capillaries were seen in these foci. The capillary endothelium showed conspicuous swelling and proliferation, so that it was sometimes difficult to distinguish microglial rods from capillary endothelium. The ganglion cells in these foci appeared swollen, sometimes with eccentric nuclei; and a minority of these cells had undergone neuronophagia. The demyelinated foci, which were most pronounced near the olive on one side (figs. 7 and 8) appeared to merge gradually with the normal white matter and actually consisted of areas in which nerve fibers had been destroyed; the cresyl violet stain revealed a dearth of nuclei, capillary swelling and slight marginal proliferation of glia. Lower in the medulla a minute focus of demyelination was seen near the cuneate fasciculus on one side, with compound granular corpuscles between the degenerating myelin fibers.

COMMENT

The pathologic evidence in this case undeniably establishes the presence of relatively mild

nonpurulent encephalitis of the medulla oblongata but fails to demonstrate an infiltrative type of inflammatory reaction in the brain above the medulla. The histologic changes in the cerebral cortex are like those observed in many instances of toxic psychosis or toxic encephalopathy, essentially edematous changes which do not seem adequately to reflect the violence of the clinical picture. The question arises whether the anatomically demonstrable mild encephalitis and the clinical picture of a toxic psychosis, with its minimal histologic substratum, were indeed produced by one causative agent, namely, the virus of herpes zoster. It might well be argued that the encephalitis of the medulla oblongata was the consequence of an upward extension of the zosteric inflammatory process beyond its traditional confines of the cervical dorsal root ganglia, and perhaps the ipsilateral regional posterior gray matter of the cord, and that, independent of the zona, the patient had a toxic psychosis, perhaps the result of pneumonia. However, the terminal pneumonia was not clinically demonstrable until a few days before the patent's death, and no other source of toxemia was revealed clinically or at necropsy. The fibrinous pericardosis was considered a terminal development.

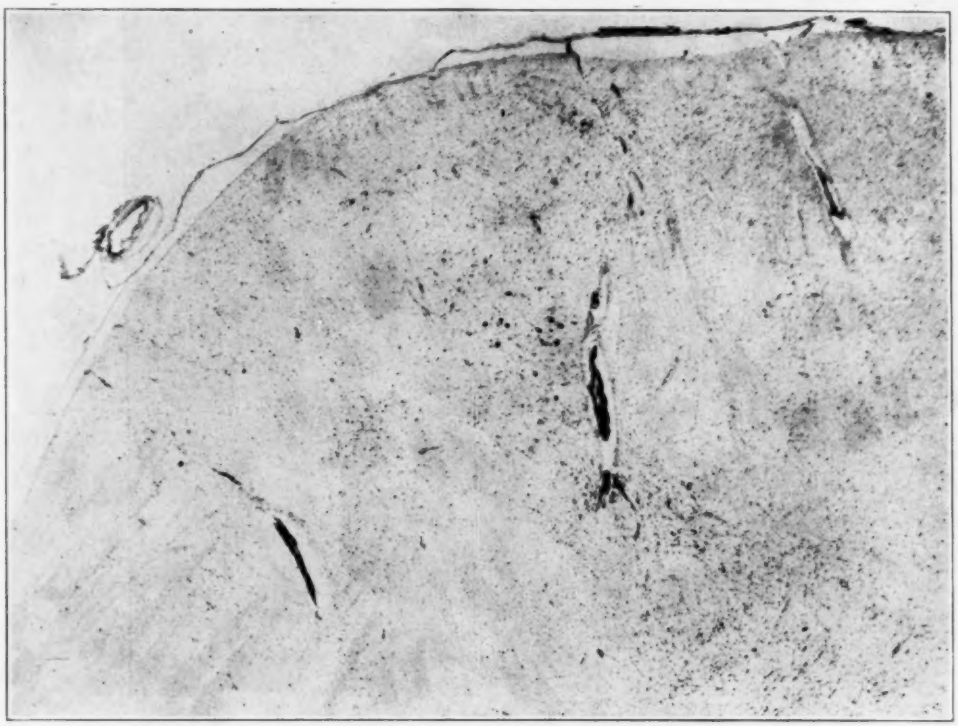


Fig. 3.—Low power view of the medulla, region of the lateral cuneate nucleus, showing perivascular infiltrations. Cresyl violet stain.

It is most reasonable to assume that the inflammatory reaction within the medulla oblongata was indicative of the presence therein of the virus of herpes zoster (after its intraneural dissemination rostrad from the ganglionitis of the upper cervical ganglia and the posterior poliomyelitis). It is plausible, furthermore, that in this apparently allergic patient the toxin of the virus of herpes zoster was the etiologic factor in the toxic psychosis or toxic encephalopathy. In this general connection, Finley,[1] in a study of the problem of pathogenesis of encephalitis occurring with vaccination, smallpox and measles, showed evidence in support of the belief that these encephalitides are allergic responses of the central nervous system to the virus of the exanthems. In our case the very mildness and the general histopathologic appearance of the changes in the medulla oblongata suggest that the process here was regressing. This is in accord with the interpretation that the encephalitis of the medulla antedated the cortical encephalopathia, the latter being an allergic complication of the former.

1. Finley, K. H.: Pathogenesis of Encephalitis Occurring with Vaccination, Variola and Measles, Arch. Neurol. & Psychiat. **39**:1047 (May) 1938.

Cases of encephalitis of presumed zosteric origin with histopathologic studies of the brain are rare. The best known cases are those of Thalhimer [2] and Biggart and Fisher.[3] In both these cases there was relatively little infiltrative inflammatory reaction in the cerebral cortex, and cerebral symptoms developed more than a month after onset of the herpes. In our case the mental symptoms appeared in the course of the receding stage of the herpes zoster, about one month after its onset.

Thalhimer's [2] case was that of a woman aged 72 who became weak and drowsy six weeks after onset of herpes zoster over the right side of the neck and died a week later. Necropsy revealed prominent perivascular areas of infiltration in the cord, with a decreasing degree of involvement through the medulla and pons, occasional foci of infiltration in the basal ganglia and none in the cortex.

Biggart and Fisher [3] described the case of a man aged 63 who five weeks before had an attack of herpes zoster involving the right buttock and thigh; the patient was drowsy and delirious on admission to the hospital and died on the fifth day. Necropsy disclosed perivascular infiltrations in the posterior portion of many segments of the cord and the lumbar dorsal root ganglia; there was slight involvement of the brain stem, the cerebellar nuclei, the thalamus, the hypothalamus and the parietal cortex. Yet the cortex in the main presented only chromatolysis.

A less convincing case of encephalitis of presumed herpetic origin was reported by Anderson and Wulff [4]; in a woman aged 80, two or three weeks after the appearance of herpes zoster of the left arm, there developed paresis of the left arm, anesthesia over the left side of the face, difficulty in swallowing and

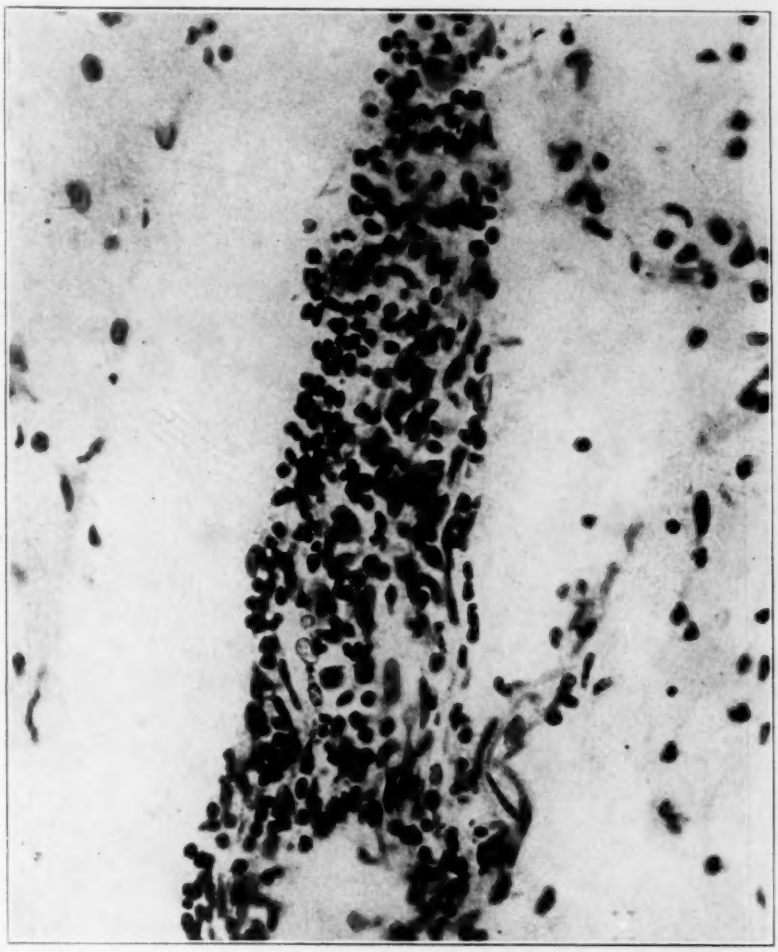


Fig. 4.—Perivascular infiltration in the caudal portion of the medulla near one cuneate fasciculus. Cresyl violet stain.

2. Thalhimer, W.: Herpes Zoster: Central Nervous System Lesions Similar to Those of Epidemic (Lethargic) Encephalitis: Report of a Case, Arch. Neurol. & Psychiat. **12**:73 (July) 1924.

3. Biggart, J. H., and Fisher, J. A.: Meningo-Encephalitis Complicating Herpes Zoster, Lancet **2**: 944, 1938.

4. Anderson, M. S., and Wulff, F.: Meningitis serosa und Encephalitis bei Zoster, Acta psychiat. et neurol. **8**:213, 1933.

speech disturbance, with an atypical Babinski sign on both sides. She died of bronchopneumonia three and a half months after the appearance of the herpes. Necropsy revealed no proliferative inflammatory foci in the brain, although sporadic lymphocytic infiltrations were seen about the pial vessels of the anterior median fissure and around capillaries of the nerve roots.

Bellavitis [5] reported the case of a psychotic patient aged 53 who had been alcoholic and in whom cutaneous herpes zoster had suddenly developed in the distribution of the second to the fourth cervical segments on the left side. Eight days later palsy of peripheral type appeared on the same side of the face, and a few days later hemiparesis developed on the left side. Necropsy revealed cirrhosis of the liver and congestion of the central nervous system, particularly the cervical posterior root ganglia on the left side. Microscopic study revealed hyperemia, hemorrhage, perivascular lymphocytic infiltration and neuroglial proliferation, especially in the cervical portion of the cord, and also in the medulla and the pons. The posterior horn cells in the cervical part of the cord appeared diseased.

Roger, Poursines and Paillas [6] reported a case of poliomesencephalomyelitis marked clinically by multiple palsies in the distribution of the cranial nerves, which developed after herpes zoster of the external ear. The patient died of failure of medullary function ten months after the onset of the illness. Necropsy revealed inflammation of the posterior gray matter of the first cervical segment and small lesions with telangiectatic proliferation in the white matter of the medulla and pons.

Schiff and Brain [7] reported a fatal case of acute meningoencephalitis associated with herpes zoster in which necropsy was not done. In a man aged 67 there developed herpes zoster, the cutaneous lesion affecting

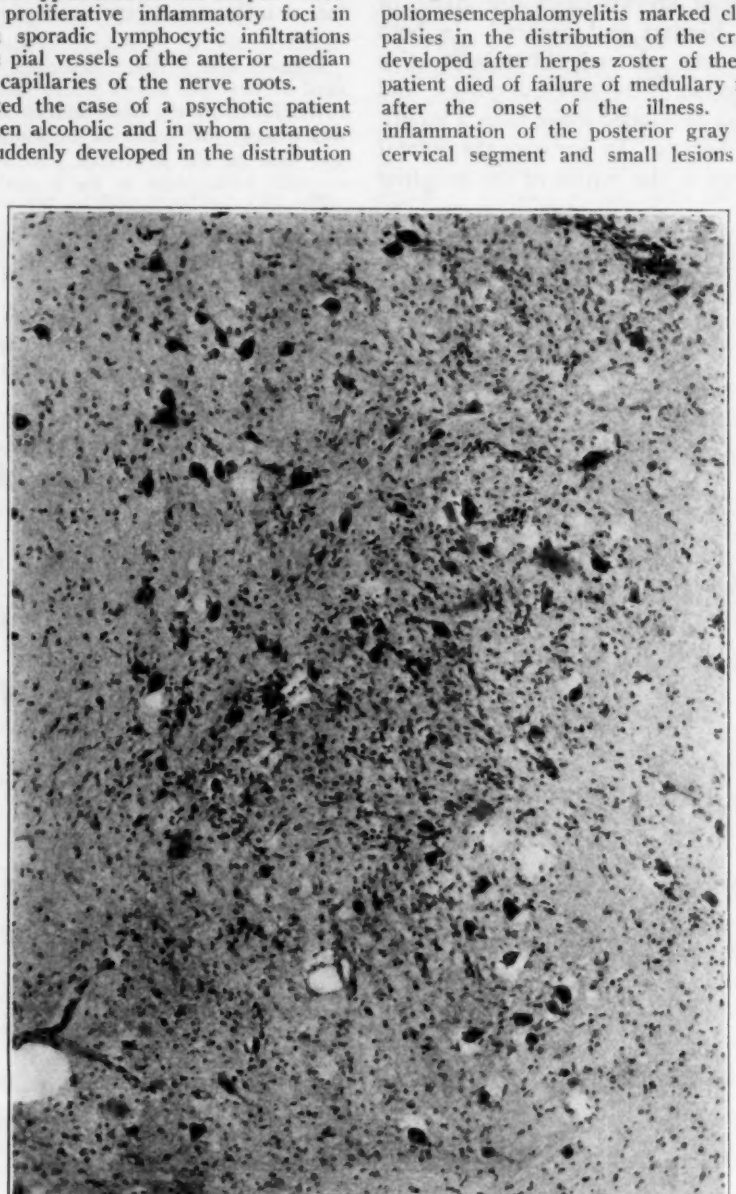


Fig. 5.—Tissue focus, showing glial and capillary hyperplasia and destruction of ganglion cells in the lateral cuneate nucleus of the medulla. Cresyl violet stain.

5. Bellavitis, A.: Nevrassite da herpes-zoster: Contribute clinico-anatomico, Riv. di neurol. **4**:337, 1931.

6. Roger, H.; Poursines, Y., and Paillas, J.: Origine zostérienne probable d'une poliomésencéphalo-myélite subaiguë, Rev. d'oto-neuro-opht. **16**:176, 1938.

7. Schiff, C. I., and Brain, W. R.: Acute Meningo-Encephalitis Associated with Herpes Zoster: A Fatal Case, Lancet **2**:70, 1930.

the right side of the lower jaw and the upper half of the neck and the occipital region on the same side. About a week later he became drowsy and confused and manifested bilateral ptosis and slight weakness of the lower right side of the face and of the right arm. The deep reflexes were absent; the plantar responses were normal. Examination of the spinal fluid revealed 120 mononuclears per cubic millimeter. The patient became comatose, the temperature remaining below 99.4 F., and died of bronchopneumonia twenty-one days after the onset of the preeruptive neuralgic pain. Two or three days before the patient's death his son, aged 32, became ill with chickenpox. The spinal fluid of the patient with herpes zoster gave a positive reaction in a complement fixation test when used as an antigen against the serum of patients convalescing from the disease.

Andre-Thomas and Buvat[8] described the case of a woman aged 58 who had been psychotic for several weeks, whereupon there developed herpes zoster of the trunk. With the appearance of the herpes the patient soon became comatose, showed rigidity of the neck (without, however, pleocytosis of the spinal fluid) and died at the end of the eighth day. Necropsy was not performed. The authors raised the question whether encephalitis may complicate herpes zoster.

Castel[9] reported the case of a man aged 42 who had herpes zoster, with an eruption over the second to the fourth cervical dermatomic area on the right side. Lumbar puncture revealed 28 lymphocytes per cubic millimeter of spinal fluid. About twenty-three days after onset of the herpes there developed peripheral palsy of the right side of the face, which gradually cleared up. However, about forty days after the appearance of the herpes, crises of dysesthesia, provoked by slight contact, occurred on the right side, and examination revealed loss of position sense in the right extremities and stereoanesthesia of the right hand. A month later paresis of the right upper extremity associated with hyperflexia was noted. At the last examination, three months later, the subjective sensory disturbances and the astereognosis of the right hand (with preservation of ordinary tactile, topognostic and vibratory sensibility) were still present. In spite of lack of anatomic verification, the author expressed the belief that the clinical signs were indicative of a lesion of the thalamus of zosteric origin.

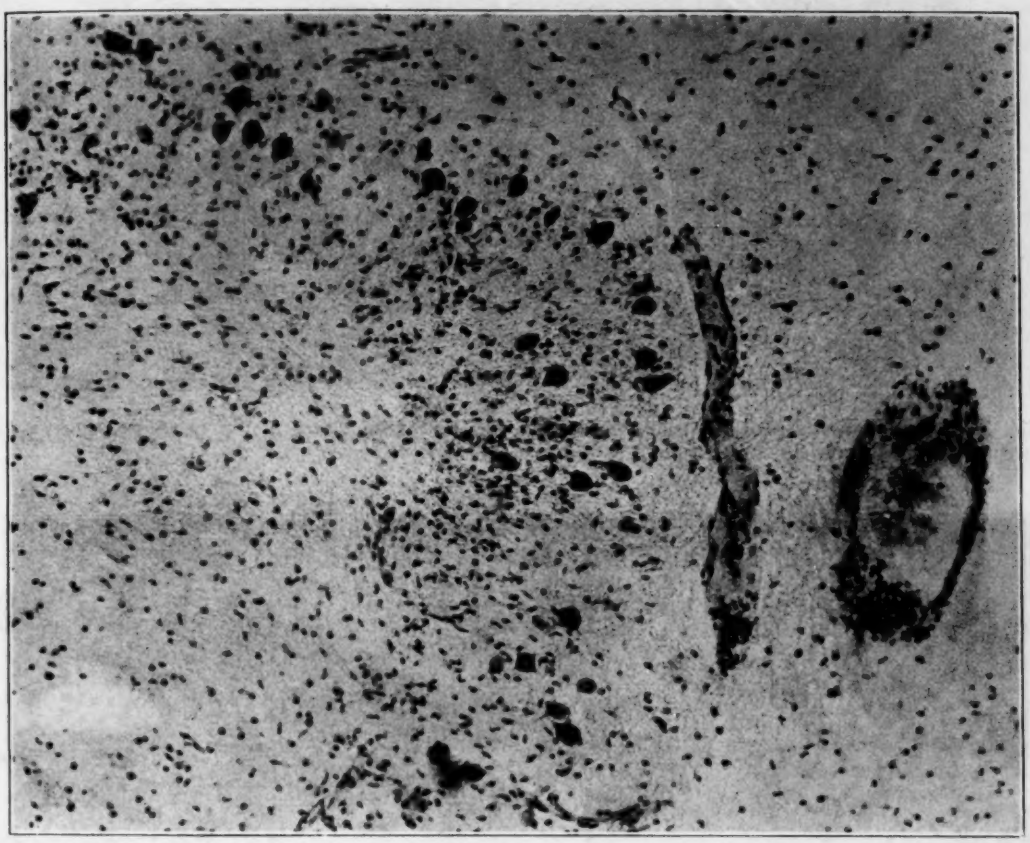


Fig. 6.—Tissue focus, marked particularly by glial hyperplasia, in the inferior olivary nucleus, with adjacent perivascular infiltration. Cresyl violet stain.

Certain similar features of the present case and of 6 cases[10] reported in the literature in

8. Andre-Thomas and Buvat, J. B.: Existe-t-il une encéphalite zonateuse? Herpés zoster à foyers multiples (mort au huitiéme jour), Paris méd. **1**:600, 1931.

9. Castel, J.: Sur un nouveau cas d'atteinte du névraxe dans le zona, Thesis, Lyon, Bosc frères, 1935.

10. Thalhimer.[2] Biggart and Fisher.[3] Anderson and Wulff.[4] Bellavitis.[5] Schiff and Brain.[7] Andre-Thomas and Buvat.[8]

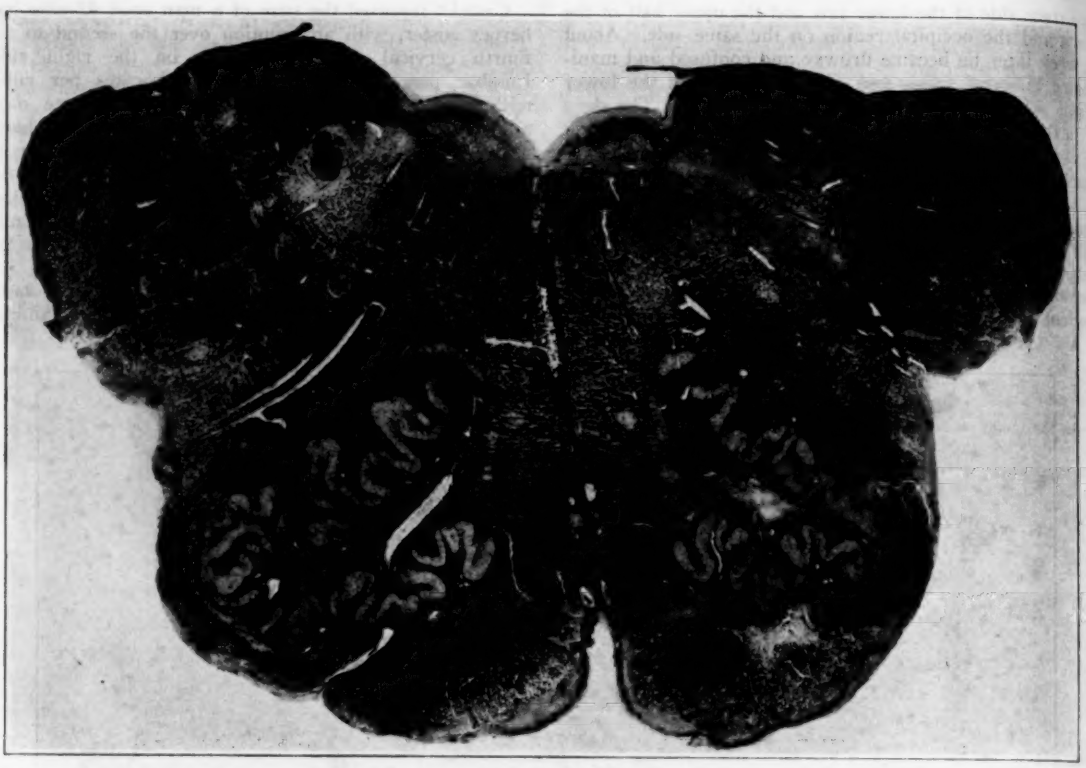


Fig. 7.—Low power view of the medulla oblongata, showing foci of destruction of myelinated fibers adjacent to one inferior olivary nucleus. Weil stain.

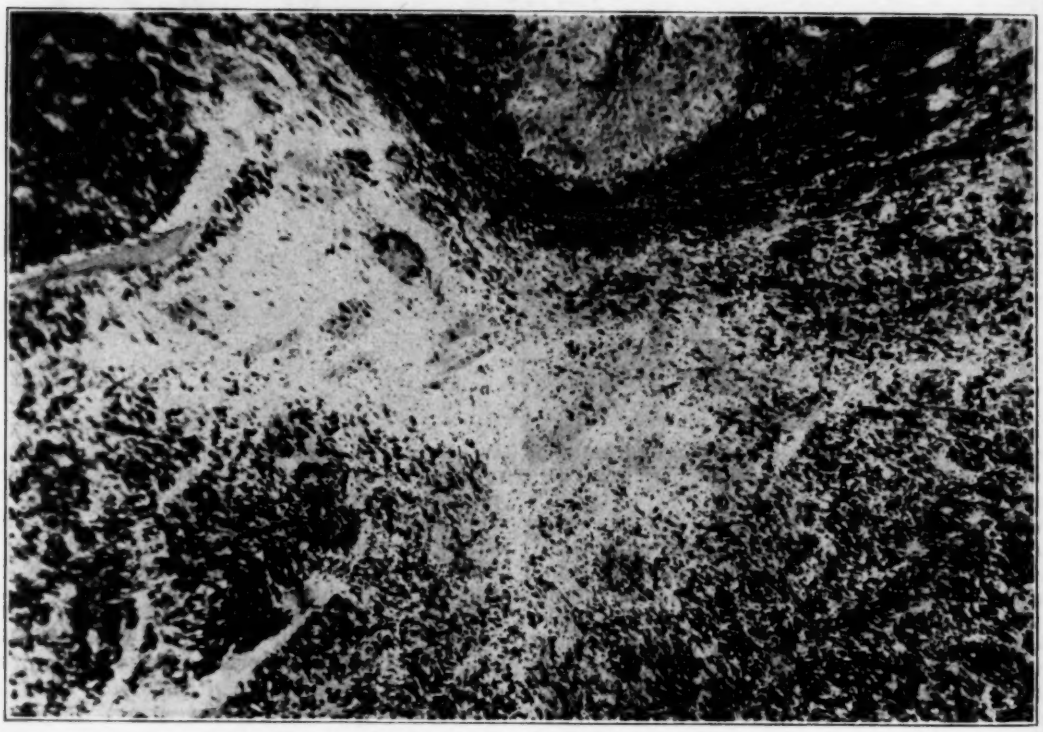


Fig. 8.—Small area of destruction of myelinated fibers adjacent to the inferior olive in the medulla. Weil stain.

which data are available are of interest. The dermatomic level of the cutaneous eruption was apparently cervical except in 1 case, that of Biggart and Fisher,[8] in which it was sacral. The interval between the onset of clinical herpes zoster and the symptoms of encephalitis was from four to six weeks in 3 cases in which the clinical manifestations were generalized (drowsiness, delirium or irrationality) and about one to three weeks in 4 cases in which the onset was with focal signs, such as facial palsy.

Herpes zoster has been noted to occur in the course of other neurotropic diseases. Thus, Netter [11] found that when herpes zoster and lethargic encephalitis occurred in the same patient, the zoster usually followed the encephalitis. In 3 of the cases reported by Netter some relation between herpes zoster and chickenpox was indicated because the latter disease developed in persons in contact with the patients.

The much discussed problem of the relation between herpes zoster and chickenpox is of some importance in this condition. Encephalitis following chickenpox is well known (van Bogaert,[12] Zimmerman and Yannet [13]) but is marked by perivascular infiltration and demyelination, especially in the cerebral and cerebellar white matter, without significant involvement of the brain stem or the cord.

SUMMARY

The amount of literature on encephalitis of presumed zosteric origin is meager but is sufficient to indicate that this complication may occur. The overflow of the herpetic inflammatory process to the efferent side of the neuraxis with facial palsy or myelitis has been well authenticated clinically. Meningitis as a complication of herpes zoster has also been clinically established. Until further cases have been carefully studied and reported, knowledge of encephalitis as a complication of herpes zoster must remain unclear. In previous cases in which necropsy was done the cerebrum, in contradistinction to the brain stem, was mildly involved by demonstrable infiltrative changes. In the present case there were no infiltrative changes in the neuraxis above the medulla oblongata, and it is suggested that the toxic encephalopathy affecting the brain proper may have been an allergic response to the virus of herpes zoster.

55 East Washington Street.

59 East Madison Street.

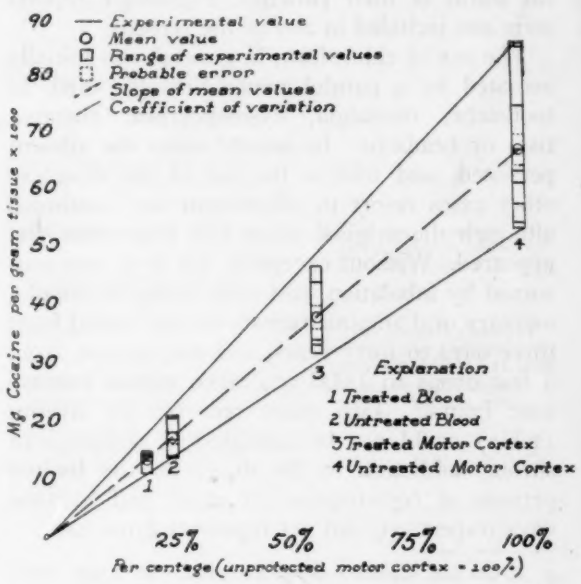
11. Netter, A.: Seize observations de zonas dans l'encéphalite léthargique, Bull. et mém. Soc. méd. d. hôp. de Paris **54**:793, 1930.

12. van Bogaert, L.: Contribution clinique et anatomique à l'étude des manifestations neurologiques et psychiatriques de l'infection varicelleuse, J. de neurol. et de psychiat. **30**:623 (Oct.) 1930.

13. Zimmerman, H. M., and Yannet, H.: Nonsuppurative Encephalomyelitis Accompanying Chickenpox, Arch. Neurol. & Psychiat. **26**:322 (Aug.) 1931.

CORRECTION

In the article by R. B. Aird and L. Strait entitled "Protective Barriers of the Central Nervous System," on page 54 of the January 1944 issue of the ARCHIVES, figure 3, page 62, is not the illustration intended for that place. The correct graph is presented herewith. The legend for the figure as given in the original article is correct.



CHRONIC CHLOROFORM POISONING

CLINICAL AND PATHOLOGIC REPORT OF A CASE

GERT HEILBRUNN, M.D.; ERICH LIEBERT, M.D., AND PAUL B. SZANTO, M.D.

CHICAGO

Motivated by interest in a case of prolonged addiction to chloroform falling under our observation, an investigation of the relative frequency of this aberration disclosed only 29 authentic cases in the literature appearing after the discovery of this drug, in 1830, and its subsequent introduction into medical science.

Twenty-four cases were reported before 1900; only 5 cases have since been recorded.[1] In the majority of the accounts neurologic data were not included, the statements being limited to the cause of the addiction and the amount and mode of consumption. Of the authors, only Friedländer,[1a] Rehm [1b] and Storath [1f] offered a résumé of neurologic observations, in addition to somewhat more specific data pertaining to the physical status of their patients. Pathologic reports were not included in any of the records.

The use of chloroform in general was initially actuated by a painful minor disorder, such as toothache, neuralgia, dysmenorrhea, rheumatism or headache. In several cases the ailment persisted, and with it the use of the drug; in other cases resort to chloroform was continued although the original cause had long since disappeared. Without exception, the drug was consumed by inhalation, and only rarely by supplementary oral administration. Its use varied from three days to forty years, and the amount, from a few drops to 1,000 cc., taken within twenty-four hours.[2] Two cases reported by Svetlin (table) could not be tabulated as instances of chronic addiction to the drug, for the limited periods of consumption of three and thirteen days respectively did not represent gross use.

The consequences of abuse of chloroform varied from a completely negligible effect to "wrecking of the physical and mental energy of the patient"; on a lesser scale, the effect was described as irritability and a propensity toward moods of depression and anxiety. Delusions, hallucinations and delirious conditions were observed, as well as emaciation, paresthesias and tremor of the hands (table). It was uniformly emphasized, particularly in the more detailed reports, that withdrawal symptoms were not encountered. The authors invariably stressed the short duration within which withdrawal and "cure" could be effected but added that the patients had frequent relapses into the old habit.

REPORT OF CASE

History.—A white man aged 33, a bookkeeper, with a creditable work record, had been addicted to the use of chloroform for twelve years. He was described by his mother as considerate, with an even, tranquil disposition. Throughout the four years of high school he had maintained excellent grades.

The addiction began twelve years prior to his hospitalization, in 1940, when, at the age of 21, he had a rheumatic attack and was advised by a pharmacist to inhale chloroform for alleviation of the pain. Within three months the pain had abated, but the patient continued to take the drug each night in 1 ounce (29.5 cc.) doses for seven years and in 2 ounce (60 cc.) doses during the five years preceding hospitalization. In August 1939, at the close of ten years of addiction, the patient grew restless and worrisome and became easily excitable. He asserted that he slept with difficulty.

"To play a prank on a friend," he turned in a false fire alarm and was arrested. After a ten day stay in an institution, he abstained from chloroform for five months. It was learned that on his resuming the habit he frequently fell wherever he might be, lapsing into heavy slumber. He falsely asseverated at this time that he maintained twelve men under his industrial supervision and fictitiously asserted that a former friend, Dr. X, often called on him. He became depressed and wept freely, rejected food and grew increasingly careless of his appearance.

The patient abruptly abandoned the use of chloroform on Dec. 19, 1940 and had a convulsion three days later. At this juncture he was rehospitalized. Pronounced ataxia of his extremities and dysarthria then developed, manifestations which, according to the history and the patient's statement, had not been observed at any previous period. On December 28 he was transferred to the Elgin State Hospital. There, during the first

From the Chicago State Hospital, the Elgin State Hospital and the University of Illinois College of Medicine, Department of Psychiatry.

1. (*a*) Friedländer, J.: Habitual Chloroform Abuse, Deutsche med. Wchnschr. **33**:1494, 1907. (*b*) Rehm, P.: Chloroform, Berl. klin. Wchnschr. **22**:317, 1885. (*c*) Schoenfeld, A.: About Chloroform Mania, Med. Klin. **28**:1272, 1932. (*d*) Toebben, H.: Chloroform Addiction in Connection with Other Morbid Desires, Deutsche Ztschr. f. d. ges. gerichtl. Med. **12**:285, 1928. (*e*) Clark, J. E.: A New Habit, M. Rec. **27**:452, 1885. (*f*) Storath: Habitual Chloroform Abuse, Deutsche med. Wchnschr. **36**:1362, 1910.

2. Meggendorfer, F.: Psychoses Due to Intoxications, in Bumke, O.: Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1928, vol. 7, pt. 3, p. 292.

few days, he conversed with imaginary persons and expressed the erroneous belief that his mother was in an adjoining room talking with strangers—an hallucinatory episode which cleared within ninety-six hours. Thereafter the patient remained in a friendly and cooperative mood, with commendable insight into his situation. For the remainder of the period of hospitalization overt psychotic symptoms were not discerned.

The vocabulary intelligence quotient on the Wechsler-Bellevue scale was 103; the Babcock efficiency index was determined to be —1.

On being interrogated as to his addiction, he answered that neither lustful sensations nor agreeable fantasies were associated with the use of chloroform and said that he indulged in the habit merely to insure a sound night's sleep.

Physical Examination.—The patient was slender and of small stature. His height was 5 feet 4 inches (162.5 cm.), and his weight 101 pounds (45.8 Kg.) (average weight, 125 pounds [56.7 Kg.]). The liver and spleen were without appreciable deviation from the normal. A loud, ringing apical first tone was observed. The blood pressure was 120 mm. of mercury systolic and 80 mm. diastolic; the pulse rate was 96 per minute.

Neurologic Examination.—Only the most significant findings will be noted. The pupils reacted to light and in accommodation. There was no nystagmus. The deep reflexes were normal. The abdominal and cremasteric reflexes were present. Cutaneous and deep sensibilities were intact. There was severe dysarthria, together with pronounced ataxic gait, coarse intention tremor of the tongue and fingers and manifest adiadokokinesis of the tongue and extremities. Romberg's sign was elicited with the patient's eyes open or closed. No hypotonia was present. Nystagmus and past pointing were elicited on rotation. Laboratory tests did not reveal anything pathologic. The spinal fluid was normal. A diagnosis of addiction to chloroform, with involvement of the cerebellar system and acute hallucinosis, was made.

In the next six weeks, under a dietary regimen of rich calories and vitamins, all neurologic symptoms appreciably diminished.

Data on Reported Cases of Chronic Chloroform Poisoning

Author	Year	No. of Cases	Daily Amount of Chloroform	Duration of Addiction	Psychiatric Symptoms	Neurologic Symptoms
Vigla [1a]	1867	1	30 Gm.	.....	"Impaired moral disposition"	
Boehm [1a]	1867	1	.....	.....	"Attacks of melancholia; ideas of persecution"	
Buechner [1a]	1867	1	.....	.....	"Periodic mania"	
Leudet [1d]	1874	1	150 cc.	10 yr.	.....	Paraplegia, which disappeared after a few months
Merie [1a]	1875	1	Every 5 days 1 lb. (373 Gm.)	.....	"Peculiar psychic behavior"	
Svetlin [1a*]	1882	1	.....	3 days	"Auditory, visual and sensory hallucinations"	Tremor; insomnia
		1	.....	13 days		
Watkins [1d]	1884	1	45 Gm.	15 yr.	"Hallucinations"	Tremor (delirium tremens)
Rehm [1a]	1885	1	Large amounts, sometimes 100 cc. in 24 hr.	Years	"Slowing of intellect; slight depression; weakness of memory"	
		1	.....	30 yr.	"Good memory and intellect, but severe deliria; suspiciousness"	
Schuele [1b]	1885	1	"Increasing amounts"	Many years	"Deliria; ideas of persecution; violence; irritability"	
Browning [1d]	1885	1	.....	Over 1 yr.	"Mental and physical wreck"	
		1	.....	5 yr.		
		1	.....	3 yr.		
		1	.....	8-10 yr.		
		2	.....	Years		
Clark [1d]	1885	1	½ pt. (236 cc.)	8 yr.	"Body and mental faculties affected"	Tremor
		1				
		3				
Connor [1e]	1885	1	.....	2 yr.		
Kornfeld-Bikeles [1a]	1893	1	15 to 20 Gm.	2 yr.	"Depressed mood"	Headaches; tremor of hands; narrow pupils; no reactions to light
Lewin [1d]	1897	1	.....	40 yr.	"Change of personality and temporary deliria"	
		1				
Schenzer [1c]	1904	1	.....	.....		
Friedländer [1a]	1907	1	20 drops	14 yr.	"Depression"	Left hemiplegia after 9 yr. of addiction, at age of 60; right hemiplegia 5 yr. later
Storath [1f]	1910	1	50 Gm.	15 yr.	"Stilted, manneristic behavior; superior intelligence"	Rheumatic pain; slight tremor of hands; no ataxia
Toebben [1d]	1928	1	20 Gm. several times a wk.	3 mo.	"Psychopathic personality; addicted to alcohol, cocaine, eucaine and procaine"	
Schoenfeld [1c]	1932	1	100 Gm.	15 yr.	"Quiet, calm, social"	

* These cases do not represent chronic addiction to the drug.

On March 2, 1941 diphtheria developed, with a temperature of 105.4 F. Forty thousand units of diphtheria antitoxin U. S. P. was immediately injected, and the patient's condition improved the next day. On that day 20,000 additional units was administered. In the afternoon the temperature rose again, from an early reading of 103 C., and, notwithstanding the administration of an additional 40,000 units, the patient died, on March 5.

Autopsy.—Autopsy, performed two hours after the patient died, disclosed severe toxic myocarditis as the immediate cause of death. Arteriosclerotic changes, either in the aorta or in the coronary vessels, were not noted. The liver was slightly larger than normal and weighed 1,515 Gm. Its firmness was moderately decreased, and the architecture of the cut surface was obscured. The spleen showed changes characteristic of sepsis.

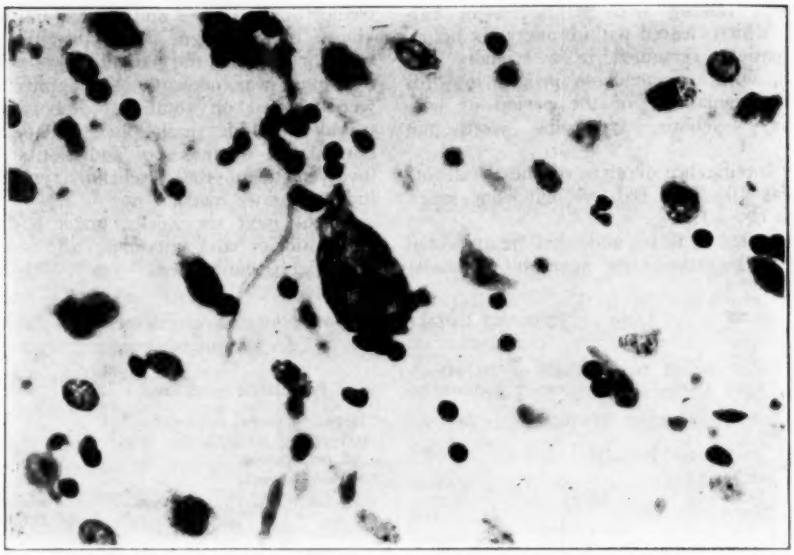


Fig. 1.—Sections of the putamen, showing numerical reduction and shrinkage of the large ganglion cells.

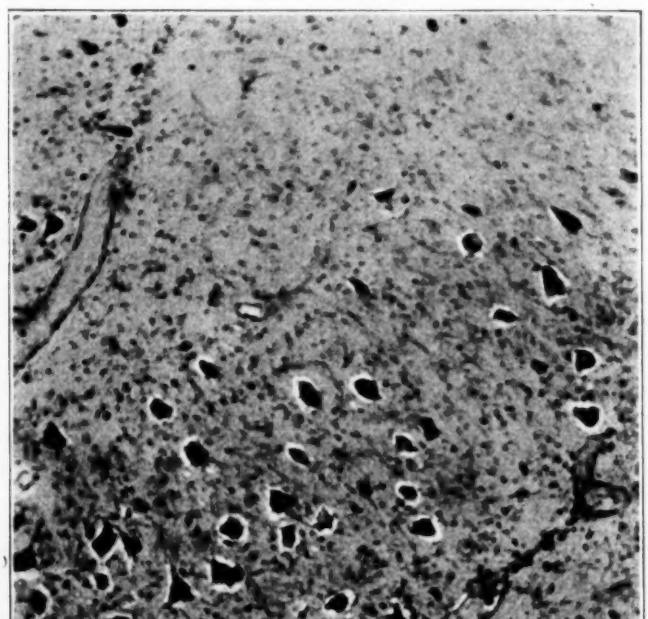


Fig. 2.—Dentate nucleus, showing numerical reduction of ganglion cells, acellular areas and shrinkage and shadow cell formation.

Microscopic Examination.—Liver: There was moderate increase of the periportal connective tissue, with round cell infiltration. The liver cells showed cloudy swelling, due to the acute infectious disease.

Brain: On removal of the brain, a negligible amount of clear cerebrospinal fluid escaped from the subarachnoid space. The meninges were smooth and glistening. The brain, which was of normal size, weighed 1,265 Gm. No evidence of localized atrophy or arteriosclerosis was observed; the basilar arteries were without essential change.

Coronal section immediately anterior to the temporal poles failed to reveal basic changes. Before the brain was fixed entire in a 10 per cent concentration of solution of formaldehyde U. S. P. several blocks were selected for frozen sections and Cajal preparations.

Fig. 3.—Cerebellum, showing numerical reduction of the Purkinje cells and moderate gliosis of the molecular layer.

Sections were taken for microscopic study from the various cortical areas, the basal ganglia, the cerebellum and the brain stem and stained with sudan IV and with the Nissl, Weil and Cajal methods. Additional Bielschowsky preparations were obtained from the cerebellar sections.

The frontal lobes presented slightly thickened meninges, with large numbers of fibroblasts and dilated blood vessels. The endothelial cells of the meningeal vessels were normal. In the perivascular spaces of the arterioles a few lymphocytes were seen in scattered fields, and the veins were moderately dilated. The architectonics of the frontal lobe was not disturbed. The large pyramidal cells in the third layer were essentially normal, except for a small number in which the nucleus was eccentrically located. In summary, a definite pathologic picture was not maintained. Examination of the remaining cortical areas yielded similar results.

The large cells in the putamen (fig. 1) had undergone numerical reduction. In many of these cells the nucleus was eccentrically located, with yellowish pigment of varying amount. The small ganglion cells were without pathologic involvement. The astroglia cells around the blood vessels were not increased. The oligodendroglia cells, which were slightly swollen, were moderately increased in number.

In the cerebellum, the most conspicuous changes were demonstrable in the dentate nucleus (fig. 2), with the cells showing moderate degenerative changes, manifested by shrinkage and poor staining quality and by reduction of their number in some fields. In certain areas the Purkinje cell count was diminished, and the number of glia cells in the molecular layer (fig. 3) was increased. Generally, however, the Purkinje and basket cells were well preserved. Bielschowsky preparations revealed that the fibers of the basket cells surrounding the Purkinje cells were unimpaired. The brachia conjunctiva remained well myelinated.

Sudan IV stains disclosed accumulation of fat in the protoplasm of certain cells of the inferior olivary nucleus, the presence of which did not necessarily indicate pathologic change. The vessels and cells of the red nucleus appeared normal.

COMMENT

A man aged 33, who had inhaled 1 to 2 ounces of chloroform daily for twelve years, experienced

a fleeting psychotic episode, requiring a ten day period of hospitalization, after approximately ten years of addiction. In the eleventh year of his addiction he began to have frequent delusional ideas and auditory hallucinations. A convulsion in the twelfth year of the habit precipitated the final hospitalization, when the patient came under our observation. He was in an acute hallucinatory and delusional state, which cleared within four days, and he remained without overt psychotic symptoms for the rest of the period of hospitalization. Such manifestations as pronounced dysarthria, severe ataxia, dysdiadokokinesis and action tremor suggested disturbance of the cerebellar system. These symptoms, with dietary control, yielded striking improvement within a few weeks. He died of diphtheria.

Histologic examination of the brain revealed moderate changes in the putamen, characterized by the presence of yellow pigment (lipofuscin) in the large ganglion cells, which were numerically reduced. Similar changes were described by Carmichael and Stern [3] in the cortical ganglion cells in cases of chronic alcoholism. In certain areas of the cerebellum the Purkinje cells and the ganglion cells of the dentate nucleus showed moderate numerical decrease, with shrinkage and poor staining quality distinctly betraying the chronic character of these alterations. Of importance, however, was the absence of edema of the brain and petechial hemorrhages in the white matter—morphologic criteria for the effect of diphtheria toxin, according to Hall.[4] The absence of these changes affords grounds for dismissal of diphtheria as the cause of the visible damage to the brain.

The moderate pathologic changes in the putamen and the cerebellum do not assuredly constitute the morphologic foundation of the neurologic manifestations observed during the initial phase of the clinical period of observation. The subsidence of these neurologic symptoms appears to be commensurate with the paucity of histopathologic signs. From Bumke's [5] notation of "shrinkage and severe changes in the ganglion cells of a diffuse type throughout the central nervous system" in cases of death due to acute chloroform poisoning, an observation in contrast to the alterations in our case, it may be surmised that the histologic changes, despite the long duration of the addiction were reversible, analogous to lesions associated with chronic alcoholism or habitual barbiturate poisoning.

SUMMARY

A man with addiction to chloroform of twelve years' duration presented acute neurologic symptoms suggesting cerebellar involvement. After a diphtheritic infection, of which he died, microscopic examination of the brain disclosed unspecific moderate degenerative changes of the ganglion cells in the putamen and the cerebellum.

6500 Irving Park Road.

3. Carmichael, E. A., and Stern, R. J.: Korsakoff's Syndrome: Its Histopathology, Brain **54**:189, 1931.

4. Hall, W. E. B.: Diphtheria and Acute Toxic Encephalitis, with Report of Case, Canad. M. A. J. **26**:566, 1932.

5. Bumke, O.: The Anatomy of the Psychoses, in Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1928, vol. 11, pt. 3.

Obituaries

GRAEME MONROE HAMMOND, M.D.

1858-1944

The passing of Graeme Monroe Hammond in his eighty-sixth year signalizes an event in the history of neurology and psychiatry in New York, since there is now only one left of that generation who represented this district among the leaders of American neurology and psychiatry.

The last male of three generations of physicians, as well as the son of one of the pioneers in the field of neurology, young Graeme had an eager, acquisitive mind. He had the prescience to fortify himself with a scientific background by first studying in the old Columbia School of Mines, class of 1878, after which he turned to medicine and graduated from New York University Medical College in 1881. He must have felt an inclination toward neurology, for shortly thereafter he became a member of the American Neurological Association, which he served faithfully and ably as secretary-treasurer for many years and as president in 1898. Medicolegal practice interested the young neurologist to such an extent that he studied at the New York Law School, graduating with the degree of Bachelor of Laws in 1897.

In 1908 Dr. Hammond became a fellow of the American Psychiatric Association and showed by his discussions at the meetings of the association a keen interest in psychiatry. He also participated actively in the meetings of the New York Psychiatric Society, of which he had been a member for many years.

He was a good teacher, possessing the knack of presenting his subject in a way that held the attention of his students. He had the chair of neurology and psychiatry at the New York Post-Graduate Medical School from 1896 to 1920.

He was public spirited and responded to every demand made on his time. In the first world war he promptly joined the Army and did excellent work in examining volunteers. Later he headed the neuropsychiatric elimination board at one of the nearby training camps. Because of his declining strength, he had gradually withdrawn from all activities during the past few years. However, when volunteers for medical control services in air raid precautions were asked for, he was one of the first to answer the call, and well I remember him at a meeting in the Seventh Regiment Armory, ready to do his bit if called on.

Dr. Hammond was a firm believer in the principle that a healthy body makes a sound mind. He always kept himself in good physical condition by some form of exercise. He was for many years the captain of the fencing team of the New York Athletic Club, and every morning early he could be seen running a mile or so before breakfast. I believe he continued this practice until his eightieth year.

For some time we have missed his kindly, genial personality at meetings. He always brought a practical, sound, common sense point of view to whatever subject he was discussing and was always courteous but firm in maintaining the position he had taken. I doubt if he ever lost his temper during a discussion, and he was never known to be aggressively sarcastic or vituperative, although there was often a strongly humorous quality to his remarks which thoroughly deflated the bombastic claims of other speakers.

His kindly spirit and undaunted courage will always be fresh in the recollections of those who knew him.

EDWIN G. ZABRISKIE.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Physiology and Biochemistry

THE DISTRIBUTION OF CHOLINESTERASE IN THE BOVINE RETINA. C. B. ANFINSEN, J. Biol. Chem. **152**:267, 1944.

By employment of single horizontal sections of the retina both for quantitative histologic analysis and for chemical study, it has been possible to determine the localization of the enzyme cholinesterase in the layers of this organ. The results indicate a predominantly synaptic localization of cholinesterase. This provides direct support for the current theory of chemical mediation of the nerve impulse. The usefulness of the retina as a test organ for the study of the general physiology of otherwise inaccessible components of the central nervous system is pointed out.

PAGE, Cleveland.

TEMPERATURE EFFECTS ON REFLEXES OF ISOLATED SPINAL CORD: HEAT PARALYSIS AND COLD PARALYSIS. M. O. DE ALMEIDA, J. Neurophysiol. **6**:225 (July) 1943.

De Almeida, in a study of the effects of variations in temperature on spinal reflexes in isolated preparations of the spinal cord of American and Brazilian frogs, found that the time of resistance of the reflexes formed curves with a maximum corresponding to a mean temperature. The position and value of this maximum depended on the climatic conditions to which the animal was accustomed. Between temperatures of 14 and 29 C. reflex exhaustion was permanent. Beyond this range, paralysis was produced by heat and cold. These types of paralysis were not due to impairment of conduction but resulted from paralysis of nerve centers by metabolic products which were ineffective at mean temperatures.

FORSTER, Philadelphia.

ELECTROENCEPHALOGRAM OF DECORTICATE MONKEYS. MARGARET A. KENNARD, J. Neurophysiol. **6**:233 (July) 1943.

Kennard studied the electroencephalogram of monkeys, obtaining electrical potentials from the cortex and the subcortical nuclei in decorticate and hemidecorticate preparations. The patterns for the cortex, the basal ganglia, the thalamus and the hypothalamus were characteristic for each area. However, each cellular complex influenced the other complexes. The electroencephalogram from the basal ganglia in a hemidecorticate preparation showed low voltage, 8 per second activity; only when the entire cerebral cortex was removed did spontaneous bursts of high voltage activity appear. The thalamic pattern presented, like that of the cortex, a component of medium rate, and occasionally records from the thalamus and the postcentral cortex were synchronous. Thalamic lesions altered the cortical pattern, especially in the postcentral areas. While the hypothalamus presented little activity, its ablation notably altered the cortical electroencephalogram. Partial ablation of the thalamus or the hypothalamus temporarily altered the cortical electroencephalogram, but only when both the thalamus and the hypothalamus had been ablated were the cortical potentials abolished.

FORSTER, Philadelphia.

SPONTANEOUS ELECTRICAL ACTIVITY OF THE THALAMUS AND OTHER FOREBRAIN STRUCTURES. R. S. MORRISON, K. H. FINLEY and GLADYS N. LOTHROP, J. Neurophysiol. **6**:243 (July) 1943.

Morrison, Finley and Lothrop studied the spontaneous activity of areas of the forebrain in cats. Spontaneous bursts of 5 to 10 per second waves similar to potentials seen in the cortex were obtained from various areas of the thalamus. These areas were chiefly those associated with the internal medullary lamina. Activity of this type was not observed in the relay nuclei. The authors conclude that areas of the thalamus have a tendency to produce spontaneous rhythmic bursts but that these areas may be under the control of a master area associated especially with the internal medullary lamina. Characteristic spontaneous activity was also recorded from other subcortical regions.

FORSTER, Philadelphia.

NOTE ON THE ORGANIZATION OF THE TACTILE SENSORY AREA OF THE CEREBRAL CORTEX OF THE CHIMPANZEE. CLINTON N. WOOLSEY, WADE H. MARSHALL and PHILIP BARD, J. Neurophysiol. **6**:287 (July) 1943.

Woolsey, Marshall and Bard studied the tactile sensory area of the anesthetized chimpanzee. Cortical responses, induced by mechanical movements of hair over various parts of the body, were amplified electrically and visualized by the cathode ray tube. The authors found that the tactile sensory area of the chimpanzee was organized in the same way as that of the monkey. All segments of the spinal cord below the eighth cervical were projected to the cortex in their spinal sequence, whereas the cervical segments were reversed *en bloc*. Thus, in the cortical sequence there are two areas of segmental discontinuity, one at the trigeminal-cervical boundary and the other at the cervical-thoracic boundary. These regions coincide with the boundary lines separating Dusser de Barenne's face, arm and leg areas.

FORSTER, Philadelphia.

THE RELATION OF AREA 13 ON ORBITAL SURFACES OF FRONTAL LOBES TO HYPERACTIVITY AND HYPERPHAGIA IN MONKEYS. THEODORE C. RUCH and HENRY A. SHENKIN, J. Neurophysiol. **6**:349 (Sept.-Nov.) 1943.

Ruch and Shenkin studied the effects of ablation of area 13 of the orbital surface of the frontal lobes in 5 Macaca mulatta monkeys. Hyperactivity appeared as early as the first postoperative day and increased to a maximum in the third or fourth week. After

this period a decrease in activity was usually encountered, but in no instance did the animal return to its preoperative state. Striking behavior deficits were apparent at least in the first postoperative week and consisted in a reduction of emotional expression, with absence of the startle reaction and a decreased fear reaction. The authors could not confirm the observations of other investigators that distractibility occurs with lesions of this region. The hyperactivity was accompanied by only a slight increase in food intake and by loss of weight. Ablation of other areas (10, 11 and 14) of the frontal lobe failed to produce the symptoms resulting from ablations of area 13.

FORSTER, Philadelphia.

Psychiatry and Psychopathology

THE PSYCHONEUROSES IN MILITARY PSYCHIATRY. JAMES A. BRUSSEL and HAROLD R. WOLPERT, War Med. **2**:139 (Feb.) 1943.

Brussel and Wolpert review the case records of all psychoneurotic patients admitted to a large station hospital during the first nineteen months of its existence. The commonest psychoneuroses encountered were anxiety states, conversion hysteria and reactive depressions. The rate of admission rose sharply after the Japanese attack on Pearl Harbor. Most of the patients had a high school education or better. The patients complained most frequently of precordial pain, nervousness, abdominal pain, "stomach trouble" and headache. The history seldom included a record of a previous admission to an institution, civil offenses, overt marital or other sexual maladjustment, suicidal thoughts or actions or fears. Patients with anxiety states and conversion hysteria often had a history of the death of some member of the family from a chronic incurable disease. Histories of psychoses, parental discord, alcoholism and criminality in the family were rare.

The authors recommend that before a psychoneurotic soldier is discharged from the Army his relatives be informed as to the nature of his illness, the therapy required and where and how it can be obtained.

PEARSON, Philadelphia.

MAJOR STUDIES ON FATIGUE. R. R. SAYERS, War Med. **2**:786 (Sept.) 1942.

Sayers gives a comprehensive review of the causes and prevention of fatigue. Fatigue results in a decrease of working capacity, a physiologic state involving changes in organic function, the formation of the chemical products of fatigue and a feeling of tiredness. It may be caused by physical overwork, but more commonly it is produced by psychologic and environmental strains: Two types of fatigue are mentioned in the literature—one originates entirely in the central nervous system; the second develops partly in the central nervous system and partly in the active muscles. The former occurs commonly; the latter is infrequent.

Physical fatigue may be (1) temporary, a feeling of tiredness which passes after a short rest and permits the resumption of work without decrease in efficiency; (2) subacute, when the reserves of energy are depleted, or (3) chronic, the final stage of overwork, which may initiate a condition of ill health.

In order to do the maximum amount of work with the minimum amount of effort, there must be complete coordination of the muscular movements with respiratory and circulatory activities. If the respiratory and circulatory responses are exaggerated, there is a useless expenditure of energy. The energic use of muscles depends on the interrelation of three factors: (1) changes in the skeletal muscles by which energy is transformed into muscular movement; (2) adjustments elsewhere in the body which provide the muscles with oxygen and the required foodstuffs, and (3) the means by which the two previous factors are bound together. Sayers points out that there is a physiologic basis for fatigue. When a muscle is stimulated repeatedly, there is first a slight fall in the amount of the contraction, followed by a regular increase in its extent, which is brought about by the action of the chemical substances produced by the contractile process. Finally the contractions diminish until the muscle ceases to respond at all. This is the state of fatigue of the muscle. Human muscle is 21 per cent efficient. If the rest interval between contractions and the weight of the load are kept constant, the extent of the contractions decreases as fatigue sets in. If the interval between contractions is long enough, fatigue is not apparent. After complete fatigue has occurred, a very long rest is necessary for the muscle to recover completely; if after complete fatigue further efforts to contract the muscle are made, the length of the period of rest necessary to produce recovery is much prolonged.

The capacity of the muscle to perform work is diminished by conditions which depress the general nutrition; e. g., loss of sleep, hunger, anemia or mental activity. When the circulation is improved and the amount of food, particularly sugar, is increased, there is an increased capacity to do work. The total output of muscular force is greater with small than with large loads. Notable activity in one set of muscles diminishes the amount of work put out by other sets.

The site of fatigue may be in the receptors, in the neuron cell bodies or in the muscle itself, in the region of the end plates and muscle fibers. Some authorities believe that the accumulation of lactic acid does not produce fatigue; they regard the production of lactic acid as a physiologic process. In their opinion fatigue is due to lack of oxygen.

Fatigue produces reduced efficiency, increased tendency to accidents and ill health. A temporary tendency to the development of accidents may be the result of lack of skill or of fatigue. A permanent tendency to accidents occurs usually in neurotic or psychopathic persons. It is clear, however, that a reduction in the number of hours of work leads to a decrease in the rate and the total number of accidents. A person should not be asked to work more than eight hours a day, or forty-eight hours per week. Perhaps forty or forty-four hours per week would be better.

Amar has summarized the science of human labor in his four laws. 1. The expenditure of energy is in proportion to the effort of the muscular contraction, its duration and its degree. 2. The expenditure of energy required to perform a given amount of work diminishes in proportion as the rapidity of the contraction increases. 3. There are an optimum effort and speed for the performance of the maximum amount of work with the minimum amount of fatigue. 4. The speed with which the muscle returns to a condition of repose is in proportion to the rapidity with which its work has been performed.

Working conditions should be arranged under the governance of these laws; i. e., the work should be

so organized that the minimum waste in effort and materials may be obtained. When such a program is combined with other health and safety programs, the number of accidents is decreased. If compulsory physical training of the civilian population were in vogue, especially of young adults, there would be an increase in efficiency and a lessened number of accidents.

PEARSON, Philadelphia.

PSYCHIATRY IN THE NAVY. FORREST M. HARRISON. War Med. **3**:113 (Feb.) 1943.

This is an interesting survey of the psychiatric program in the medical department of the Navy. The incidence of mental disease is relatively low, while the invaliding rate is high. The psychoneuroses, of course, form the largest group of mental diseases. Hysterical paralyses are rare. Harrison describes the organization for the exclusion of the mentally unfit and points out that proper screening at the time of enlistment is doubly important because many psychoneurotic men try to enlist in the Navy, and are even sent by their physicians to enlist in order to obtain a cure for their neurosis. Careful exclusion of the mentally unfit is necessary, for the complex and demanding naval life tends to bring out inherent weaknesses in the personnel.

Naval medical officers receive special instruction in psychiatry, and the Navy also has a definite program for the procurement of trained reserve psychiatrists and psychologists. Invaluable aid is rendered by the American Red Cross, which forms the psychiatric social service of the Navy.

The psychiatric service is valuable also in classifying the enlisted and commissioned personnel according to mental characteristics and in relating special abilities to specific tasks, so that each man may be in the position of maximum usefulness.

One of the most serious problems facing psychiatry in the Navy is the development, maintenance and improvement of morale both in peace and in war.

PEARSON, Philadelphia.

PEPTIC ULCER AT FORT GEORGE G. MEADE, MARYLAND. CHARLES A. FLOOD, War Med. **3**:160 (Feb.) 1943.

On the basis of his experience with patients suffering from peptic ulcer whom he saw at a station hospital during the past year, Flood evolved a plan of management for such patients in the Army. Most recent inductees respond poorly to treatment, both symptomatically and roentgenologically, while soldiers of the regular Army, with many years' service, respond well because they are usually of stable personality. Delayed healing of the ulcer is due usually to an associated anxiety state.

PEARSON, Philadelphia.

ACUTE EMOTIONAL DISTURBANCES IN TORPEDOED SEAMEN OF THE MERCHANT MARINE WHO ARE CONTINUING AT SEA. SYDNEY MARGOLIN, LAWRENCE E. KUBIE, MARK KANZER and LEO STONE, War Med. **3**:393 (April) 1943.

This report is based on the study at one or more interviews with 40 seamen who had been on torpedoed ships but who had volunteered to ship out again in spite of whatever inner turmoil they had suffered. It was possible to make some tentative statistical correlations between the severity of the reactions to the catastrophe and the evidence of previous mental illness, the age, years at sea, type of work, marital status, racial and natural origin, degree of alcoholism, type of ship and position of the sailor on ship at the time of the catastrophe. The authors summarize their results and draw the following conclusions:

1. Severe persistent reactions offer a poor outlook for ultimate recovery.

2. Pathologic alcoholism or a history of a previous psychiatric illness predisposes to the occurrence of severe and incapacitating reactions.

3. Severe reactions occurred with the highest degree of frequency among the Anglo-Saxon, Scandinavian and continental European members of the steward's department and with lowest frequency among the Latin-Americans and Negroes of the same department.

4. Persons in the age period of 45 to 60 seem to be especially susceptible to severe reactions.

5. There was a suggestion that severe reactions are less common among married seamen.

6. Severe reactions were surprisingly high among seamen from tankers.

7. There was surprisingly little correlation between the position of the seaman on the ship at the time of attack or the severity of the experience as a whole and the severity of the after-effects. This suggests that variations in the external situation play a lesser role in determining severe reactions than do deep-seated endopsychic factors.

The authors attempt to explain the difference in the severity of the reactions between the northern European races and the Latin-Americans and Negroes by pointing out that it is customary to force members of the two last-mentioned races into employment in the steward's department; therefore those employed there are a fair sampling of their races, while it is so unusual for men of the northern European races to seek this type of work that those who do so participate because of some endogenous psychologic quirk.

The authors were impressed by the following personality traits of the group. The men tended to be small in stature, thin, wiry, gnarled and underfed. They were fairly consistently friendly and grateful for the interest shown in them. They were better read than most of a comparable group of working men. A majority had gone to sea early in life, and their motivation seemed to be a strong, inarticulate need to get away from home and the disciplined social authority and regimentation of life on land. This was so strong as to approach the status of a land phobia. More than half of the men were single, divorced or separated from their wives. Overtly, the majority were predominantly heterosexual, but the heterosexuality ranged from promiscuous relations with prostitutes to intense transient attachments to some kindly mother figure.

There was a hungry quality to the yearnings expressed which was often in poignant contrast to the history of rebellion against home and to the compulsive pattern of runaway lives.

Their political, social and economic attitudes were as divergent as could be found among any group of men. They were intent on service in the war effort and had a striking sense of loyalty to and pride in their union. Their independence and self sufficiency made them prickly toward the additional disciplinary and quasimilitary relations between the officers and men due to the exigencies of war. They were acutely

sensitive to the manner of their reception in foreign ports. They resented the inattentiveness of the British, which they contrasted sharply with the friendliness with which they were received in Russian ports. Bitterness in any form was rare, and in general criticisms were elicited only after considerable questioning.

PEARSON, Philadelphia.

MORALE. LEONARD R. SILLMAN, War Med. **3**:498 (May) 1943.

Sillman points out the need for the emotional conditioning of American soldiers for the battle situation. He believes that the soldier should be presented with a clear decisive formulation of why he has been placed on the battlefield and why he must conquer or die. Such a formulation should be combined with a slogan. Every technic possible should be used to get him to embrace this formulation passionately. Of course, such measures will stir deep emotions of hate and revulsion against the enemy, but this is necessary to give the soldier the psychologic resources necessary for the successful prosecution of the most harrowing experience of life, namely, war. Psychiatrists have found that soldiers who enter a campaign out of conviction suffer much less from war neurosis than those who do not.

Sillman points out that the American war effort cannot afford to continue to ignore the knowledge which psychoanalysts and psychiatrists have about anxiety, panic, aggression, submission, death, fears, etc.

PEARSON, Philadelphia.

AMBLYOPIA IN HYSTERIA. VINCENT P. MAHONEY and WILLIAM O. LINHART, War Med. **3**:503 (May) 1943.

Mahoney and Linhart studied 13 patients with hysterical amblyopia, whose cases they classified under (1) the acute, (2) the chronic and (3) the mixed form. Psychobiologic studies revealed that they were constitutionally immature, emotionally defective, resigned to their fate and poor in intellectual endowment. The predominating symptom in this series was referable to the visual apparatus. With 1 exception, all the patients gave lifelong histories of poor vision, beginning in the first three grades of school. Perimetric examinations showed concentrically contracted visual fields in all cases. The authors conclude that men with this form of amblyopia should not be inducted. When they are discovered in the armed services, they should be referred to a psychiatrist for disposal.

PEARSON, Philadelphia.

Treatment, Neurosurgery

RADIOGRAPHIC CONTROL FOR PARAVERTEBRAL INJECTION OF ALCOHOL IN ANGINA PECTORIS. JAMES C. WHITE and ROBERT W. GENTRY, J. Neurosurg. **1**: 40 (Jan.) 1944.

The results of paravertebral infiltration of procaine and alcohol in the treatment of intractable angina pectoris is satisfactory if the upper three or four thoracic ganglia and their rami are thoroughly impregnated. In 85 per cent of a series of 20 cases reported by White and Gentry good results were obtained by following the indicated technic. The chief difficulty lies in the accurate insertion of the needles, especially in the upper two ganglia. This difficulty has been overcome by checking the position of the needles after they have been inserted, by means of a portable x-ray machine.

WHITELEY, Philadelphia.

CEREBROSPINAL RHINORRHEA: SURGICAL REPAIR. WILLIAM J. GERMAN, J. Neurosurg. **1**:60 (Jan.) 1944.

Cerebrospinal rhinorrhea is said to be a relatively common complication of craniocerebral injury in the frontal region. Spontaneous recovery may occur as late as eight weeks after the injury, and the condition may develop after an interval of several weeks. In cases of the chronic condition surgical repair is always advisable.

German describes a method of repair which has been employed successfully for the past five years. It utilizes a dural flap from the crista galli to cover the defect in the cribriform plate. The author reports 5 cases in which this procedure was used with success. Medication with sulfonamide compounds is given for an appropriate period before and after operation. There were no recurrences of the rhinorrhea, and in only 1 case did meningitis (sterile), with mild fever and pleocytosis, develop.

WHITELEY, Philadelphia.

THE CHEMOTHERAPY OF INTRACRANIAL INFECTIONS: IV. THE TREATMENT OF PNEUMOCOCCAL MENINGITIS BY INTRATHECAL ADMINISTRATION OF PENICILLIN. COBB PILCHER and WILLIAM F. MEACHAM, J. Neurosurg. **1**:76 (Jan.) 1944.

Meningitis was produced in several groups of 10 to 14 dogs each by injection of type I pneumococci into the cisterna magna. Half of each group of animals were treated with penicillin, and the remaining half were used as controls. A total of 96 experiments were performed.

In the first series (48 experiments) 50 units of penicillin was injected intrathecally daily, with slight, but definite, improvement as compared with the condition of the untreated controls. In the second series, of two groups of 12 dogs each, doses of 100 and 200 units of penicillin respectively were injected intrathecally daily; almost half the treated animals survived, and most of the deaths were due to lobar pneumonia. Because of the resulting pneumonia, a third series (24 dogs) were treated with the intrathecal injection of 200 units of penicillin daily and the intravenous injection of 1,000 units three times daily; the results were even more favorable than those in the second series.

WHITELEY, Philadelphia.

THE USE OF PRODUCTS PREPARED FROM HUMAN FIBRINOGEN AND HUMAN THROMBIN IN NEUROSURGERY. FRANK D. INGRAHAM and ORVILLE T. BAILEY, J. Neurosurg. **1**:123 (Jan.) 1944.

Ingraham and Bailey discuss the progress made in solving two important neurosurgical problems: hemostasis and the prevention of meningocerebral adhesions. Fibrin foam has been developed as a hemostatic agent. It is a dull, porous material, slightly brittle, which in the dry state is composed of dense strands of fibrin fibers with air spaces, which may easily be seen with the naked eye. At the operating table the dry matrixes are soaked in a solution of human thrombin and are then applied to the bleeding surface. This application is instantly effective in hemostasis, whether with simple surface bleeding or with bleeding from deep venous channels. The advantages of the procedure are chiefly two: first, the shortening of many neurosurgical pro-

cedures and, second, the facilitation of many operations which had heretofore been impossible or too difficult because of profuse bleeding or diffuse distribution of the lesion. Histologic studies in human and animal experiments have proved that the foam is rapidly absorbed, with minimal or negligible tissue reaction, even in conjunction with the employment of sulfadiazine and penicillin.

The authors discuss, also, the use of a substitute for the normal human dura mater-fibrin film: This substitute is a strong, smooth, translucent, uniform sheet with considerable elasticity. There are two principal uses for such a substitute: first, in the plastic repair of dura mater removed either by trauma or by operation and, second, in the prevention of meningocerebral adhesions, an important factor in posttraumatic convulsions. After animal experiments revealed the absence of tissue reaction, the absence of adhesions, the retention of the subdural space and the replacement of the film by a neomembrane of fibrous tissue, studies on human subjects were begun. Fibrin film has been removed at second operation or at autopsy at intervals varying from fourteen hours to eighty-one days; in no case was there any inflammatory reaction or evidence of adhesions. Concomitant use of sulfadiazine and penicillin did not result in any change in tissue reactions.

The authors conclude that, on the basis of present evidence, fibrin film is superior to other materials previously tested.

WHITELEY, Philadelphia.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY, AND NEW YORK NEUROLOGICAL SOCIETY

GERALD R. JAMEISON, M.D., *Chairman, Section of Neurology and Psychiatry, Presiding*
Joint Meeting, Feb. 8, 1944

Disturbances in Sleep Mechanism: A Clinicopathologic Study. DR. CHARLES DAVISON and CAPTAIN EDWIN L. DE MUTH (by invitation).

Disturbances of sleep, consisting of insomnia or hypersomnia, may be divided into two main groups: disorders associated with lesions of the nervous system and psychogenic disorders. Attempts at correlation of this mechanism on a neuroanatomic and physiologic basis in man have led to various interpretations. The problem is beset with many difficulties because the lesions in many of our cases, and in cases reported by other authors, were neither isolated nor limited to specific areas in the nervous system. This is especially true of cases of somnolence associated with cerebrovascular and other diseases with bilateral or multiple lesions of the central nervous system. The localizing area responsible for this physiologic deviation may be determined with difficulty, even in cases of a single neoplastic lesion, because the growth may cause widespread disturbance in function through compression of other structures or through interference with the cerebrospinal circulation. A careful evaluation, however, of the clinical symptoms and the location of the significant lesion may help in a reconstruction of the localizing area and the important centers and pathways responsible for hypersomnia or insomnia.

As will be demonstrated, disturbances in sleep may occur with lesions at various levels in the nervous system, from the cortex to the medulla oblongata. There is experimental evidence indicating the possible location of these lesions in man. Although the hypothalamus seems to be the chief center controlling this function, it is well to remember that by means of its pathways the hypothalamus is in intimate connection with the cortex, the thalamus, the basal ganglia, the mesencephalon and the brain stem. A lesion in any of these centers or along their hypothalamic connections may account for the disturbance in the sleep mechanism. The disintegration of this mechanism may be caused by either destructive or irritative lesions or by psychogenic factors. Psychologic disturbances most likely depend also on interference with the centers and pathways to be described.

From the nosologic point of view, disturbances in sleep should include the various designations used, such as lethargy, somnolence, stupor, coma and unconscious states. Some observers have expressed the belief that these states are separate entities instead of various phases or stages of the same disturbance, regulated by the same centers and the same pathways. They have asserted that hypersomnia or somnolence should be differentiated from stupor, for the patient can be easily aroused from the former and when so aroused appears to be in complete possession of his senses.

Approximately 300 cases of disturbances in sleep mechanism were studied clinically, and autopsy was performed in 50 cases. In most of these cases the disturbance was the result of a neoplasm; in other cases a vascular or other disease of the nervous system was the causative factor. The cases, however, are described as far as possible in accordance with the location and the level of the lesion.

Level of Lesion	No. of Cases
Cortical	8
Corticodiencephalic	20
Diencephalic (hypothalamus)	17
Mesencephalic-metencephalic	5

A number of cases of diffuse lesions in the cortex, diencephalon, mesencephalon and metencephalon are omitted from this presentation because they would be confusing from the point of view of localization. The case of a patient with narcolepsy in which electroencephalographic studies were made illustrates the importance of the psychologic factors in the sleep mechanism.

In every case reported observations were made during the period of sleep disturbance. A number of questions were asked and attempts made to arouse the patient, as indicated in the brief history of each case. The few cases in which the patient was in deep coma and could not be aroused are not included in this presentation. As increased intracranial pressure, endocrine disturbances, ocular manifestations and other features have been claimed by some observers to play a role in sleep disturbances, special attention has been given these factors in the evaluation of their importance.

Illustrative cases from each group are presented. From the analysis of our clinicopathologic material, the cases reported in the literature and the results of animal experimentation, it is possible to reconstruct in part the centers and their connections which regulate the sleep mechanism, despite the insufficient evidence for some of the hypothalamic pathways. A neuroanatomic and neurophysiologic review of the subject is presented.

Although the evidence indicates that the hypothalamus is undoubtedly one of the chief centers for the control of sleep or wakefulness, other centers have to do with this mechanism. Our cases of diseases of the cortex and mesencephalon demonstrate that these structures must be in intimate connection with the hypothalamus and with other centers for the regulation of sleep. Interruption of these pathways to and from the hypothalamus may lead to interference with the same mechanism.

Narcolepsy as a Psychogenic Symptom. DR. LEO A. SPIEGEL (by invitation) and DR. C. P. OBERNDORF.

A housewife aged 50 had had attacks of uncontrollable sleep for two years. These attacks were of variable duration; some lasted only a few minutes and others many hours. They were preceded by polydipsia and were frequently accompanied by cataplexy. At first a lesion affecting the hypothalamic area for sleep was considered, but psychiatric investigation revealed that the patient's condition belonged to the group of hysterical narcolepsies. The etiologic background for her symptoms was a complex, intrafamilial sexual relation-

ship, which began at the age of 6 years and was maintained for forty years. Solely by means of the cathartic procedure, as originally described by Freud, it became possible to rid the patient of her attacks of compulsive sleep, cataplexy and polydipsia. The disappearance of her narcoleptic attacks was followed by a profound sense of guilt, an occurrence suggesting that the function of the attacks of sleep was to allay this sense of guilt. From the point of view of therapy it is suggested that in selected cases the simpler methods of the early days of psychoanalysis may be more fruitful than the complex methods of modern psychoanalysis. The induction of sleep in this patient through the recall of traumatic memories and its dissipation through catharsis suggest the physiologic processes of inhibition and disinhibition, as described by Pavlov.

DISCUSSION ON PAPERS BY DR. DAVISON AND CAPTAIN DE MUTH AND BY DR. SPIEGEL AND DR. OBERNDORF

DR. SAMUEL BROCK: Dr. Davison and Captain De Muth have presented an excellent survey of the neuroanatomic and neuropathologic observations in cases associated with disturbance in the sleep mechanism. They have attempted to evaluate the various views relating to the parts played by the different segments of the central nervous system in this complex function. The authors have spoken of a voluntary control of the sleep mechanism by the cortex. With this I take partial issue. Sleep is essentially uncontrolled by the will, and while one may prepare oneself for sleep, one cannot speak of voluntary control without a good deal of reservation. Sleep is essentially a complex vegetative phenomenon, and the governing mechanism, I believe, is not the cortex but, rather, diencephalic and mesencephalic centers, in which are concentrated many other vegetative functions. The fact that certain drugs may induce sleep or wakefulness in thalamic and decerebrate animals indicates without question that the lower vegetative centers are the controlling agencies under physiologic conditions. That other parts of the central nervous system, such as the cerebral cortex, suffer modification or extinction of function is obvious.

Until recently there has been little insight as to how such a mechanism, situated in the diencephalon and the mesencephalon, can bring about sleep. Perhaps a clue is afforded by the work recently done on cerebral concussion. The unconsciousness brought about by injury to the brain has points of resemblance to sleep. In fact, Geoffrey Jefferson, the English neurosurgeon, speaks of traumatic unconsciousness as "parasomnia." Jefferson also stresses the part played in this condition by lesions in the region "extending caudally from the upper half of the fourth ventricle to the hypothalamus cephalad."

Some of the members of these societies may have heard Dr. Earl Walker, of Chicago, in December 1943, when he presented evidence to the effect that posttraumatic unconsciousness in animals is associated with extinction of cortical function, as revealed by electroencephalographic studies (Diagnostic Value of Electroencephalography, ARCH. NEUROL. & PSYCHIAT. **51**:203 [Feb.] 1944). May one not speculate on the possibility that the large correlation center, described by various authors, acts as an "electrical extinguisher or modifier," controlling and affecting widespread areas of the cortex and other parts to produce this remarkable phenomenon called sleep? Of course, inhibition in this sense, and on such a widespread scale—rhythmic in tempo, delicate in its response to various internal stimuli and external effects—is a phenomenon that still requires a great deal of study.

In disease, more especially in the narcoleptic-cataplectic syndrome, remarkable dissociations occur in the various elements making up sleep. Perhaps the most remarkable of these dissociations is the cataplectic deposturing produced by emotion. This represents the physical component of sleep dissociated from the mental and is accounted for by loss of function in lower centers. Indeed here, again, one has support for the view that thalamodiencephalic and mesencephalic mechanisms are the main activators of sleep and wakefulness, to which other parts of the central nervous system are subservient.

The remarkable case report presented by Dr. Spiegel and Dr. Oberndorf is difficult to discuss in a short period because of its many implications. The narcolepsy exhibited by the patient was seemingly conditioned by psychogenic factors. Yet one is beset by two pressing questions: Why did the patient make use of this particular, rare, conversion phenomenon, instead of using the much more common forms of paralysis? Why did the symptoms begin so late in life, i. e., at the age of 48, since the psychogenic factors went back many years? One wonders whether there was not a structural determinant in the diencephalon, since the patient exhibited other vegetative phenomena referable to nearby centers, such as polydipsia and pallor. This, of course, might lead to a formulation of the clinical picture as one compounded of psychogenic factors and an organic substrate. There can be no doubt that the usual idiopathic narcoleptic-cataplectic syndrome is an organic disease, since various observers have described oculomotor paralysis with diplopia and the Babinski toe sign during the seizure. Perhaps one seldom sees cases like the one described because the combination of psychogenic factors and adequate organic background is rare.

DR. S. P. GOODHART: Dr. Brock has ably discussed the localization and nature of the mechanism of sleep, with especial reference to its neurophysiology. The authors of the papers are highly qualified to discuss the psychosomatic relationships and are identified with studies both in organic pathology and in dynamic psychology. The relation of psyche to soma has given rise to many theories with respect to brain and body function. It was Hippocrates who first maintained that the brain is the seat of the mind, the source of intelligence, of volition and of bodily activity.

Dr. Davison's paper is a highly concentrated discussion of both physiologic and pathologic sleep. He speaks of the psychogenic and the organic basis of narcolepsy; this at once raises the question of what constitutes organic and what psychogenic.

As to the location of the sleep mechanism, clinical and pathologic investigations by Davison and others make it clear that because of the relations of nerve tracts and nerve centers to each other, both anatomic and physiologic, precise localization is speculative. Studies of large series of cases by Davison and others, including the cases which Dr. Davison presented this evening, confirm the fact that even fairly discrete lesions do not always permit functional interpretation. His series of cases, like many reported in recent literature, indicate that the disturbances of sleep may result from lesions at various levels, from the cortex to the metencephalon. The frontal lobe seems to have a definite relation to the physiology and pathology of sleep. I have seen neoplasms of the frontal lobe the initial symptom of which for a long period was a striking tendency to somnolence.

There are indeed many theories as to the mechanism of normal and pathologic sleep. The one that strongly appeals to me is that of Pavlov, who regarded sleep as a series of conditioned reflexes dependent on cortical control and cortical inhibitions. There is convincing evidence that the hypothalamus and the periventricular region of the third ventricle have a definite relation to sleep; I believe it to be an automatic center, so to speak, but I feel that the mechanism of the cortex and the anatomic connections with the diencephalon are the sources of physiologic production of sleep, both in its normal and in its pathologic manifestations. I cannot agree with Davison and the authors who maintain that stupor and coma, levels of unconsciousness, are phases of what is called the sleep mechanism. These pathologic conditions, especially the states resulting from trauma, have, in my opinion, little if any relation to normal sleep.

There is something to be said for the theory propounded by Ramón y Cajal, who expressed the belief that ameboid movements of the dendritic elements of cortical cells and transcortical fibers may be the determinants in the production of sleep; according to this theory, contact is established and broken by these physical movements.

The presentation by Dr. Spiegel and Dr. Oberndorf is an excellent and thorough study. The authors, wisely perhaps, have not given all the sordid details and the bizarre sexual perversions that doubtless were of etiologic influence in the development of this unusual clinical picture. The case offers subtle problems in psychosomatic relationships. In my opinion the case is not one of true narcolepsy, in the strict sense in which that term is used, nor do I feel that the clinical signs are entirely psychogenic. I prefer to speak of narcoleptiform seizures; neither the age of the patient nor the length of the individual attacks conforms to the usual brief or momentary periods of sleep seen in cases of true narcolepsy. There is much in the history of this case to suggest an organic change in the periventricular area of the third ventricle. The extensive nevi of the body, suggesting the presence of neurofibroma; repeated polydipsia, vomiting and headache over an extended period; prolonged attacks of somnolence from which the patient could not be aroused—all these suggest an organic pathologic process. The unquestionable psychogenic influence, as shown by the characteristic hemisensory syndrome, was, without doubt, a dominating influence in many of the symptoms. The authors of the paper apparently consider the entire picture psychogenic.

Of the therapy used, hypnosis seems to be of value in bringing out the amnesia and the dream content, and on this effect—the authors base their procedure in the long-continued application of catharsis, as outlined by dynamic psychology. It would seem that in this case hypnosis touched only the surface and did not reach the deep psychologic makeup of the patient so that she could handle her own situation and thus become conscious of, and reconciled to, her past experiences. I recall a case at Montefiore Hospital in which the hypnosis brought about a restoration, although it was only temporarily maintained; the patient might well have been permanently cured had psychoanalysis followed hypnotic therapy. The young man presented a postencephalitic parkinsonian syndrome, with the characteristic facies, salivation, suppression of normal associated movements, rigidity and tremor; because of certain other physical signs, however, my associates and I suspected a psychogenic influence. While the patient was under hypnosis and subsequently the signs and symptoms disappeared. All therapeutic measures were discontinued for three weeks, and the patient lapsed into his former pathologic state. The case raises many questions of the relation between psyche and soma and between the functional and the organic.

DR. CHARLES DAVISON: I wish to thank Dr. Brock and Dr. Goodhart for their discussion. I must disagree, however, with Dr. Brock about the volntary control of sleep. I believe, and he will agree with me, that sometimes, especially in emergency situations or during emotional strain, one can go to sleep or keep awake as one wishes. There are numerous illustrations, for instance, the marathon dancers who manage to keep awake for hours at a stretch in order to perform their act. Soldiers have been known to remain awake for two to three days or longer when required. Then there are the historical instances, such as those of Caesar, Napoleon, Goethe and Freud, who could go to sleep or keep awake voluntarily. Our first group of cases, in which there was cortical involvement, illustrates that the cortex is the representative for the voluntary control of the sleep mechanism, the chief center of which is situated in the hypothalamus. Forced wakefulness or diurnal sleep is a cortical and therefore a voluntary function. The cortex may either activate or inhibit the function of the hypothalamus. The reverse may also take place.

With regard to Dr. Goodhart's question about stupor, coma and other unconscious states, I believe that these states are phases of an exaggerated form of sleep disturbance and are regulated by the same centers and pathways. Frequently these terms are misused in clinical observations. The patient may be only lethargic and can be awakened if an attempt is made to do so; yet the record may describe him as in stupor or coma.

DR. C. P. OBERNDORF: I am not in a position to discuss the physiology of sleep because I am neither a physiologist nor an anatomist; so I shall confine my comments to our case. Perhaps I may begin by noting, in connection with Dr. Davison's comment on psychogenic factors, that there is no reason that a person with deep conflicts may not have encephalitis. The conflict would continue after, as well as before, the trauma to his central nervous system. Thus, a psychoanalyst reviewing such a patient's history would inevitably uncover these conflicts; the patient Dr. Davison reported on seems to have harbored every known tendency—from exhibitionism to incest. Therefore I do not think that his case is particularly cogent to the problem which we have presented, namely, the psychogenic factors in narcolepsy.

Dr. Brock asked why the patient did not manifest paralysis or some other symptom rather than narcolepsy as a result of her conflicts. It is not always easy to determine the nature of hysterical symptoms or the reason for the development of the particular symptom. To be sure, this patient did have a hemiparalysis. It was one of the signs which confused the diagnosis because her right hemiplegia may have been organic in origin. Perhaps complete paralysis would have meant death. Sleep, indeed, may have been a compromise symptom in preference to death, if one wishes to speculate why the somnolence developed as a symptom rather than a more serious or painful one.

One might emphasize that this patient had been ill with migraine headaches and nausea for twelve years before development of the narcolepsy. Why the narcolepsy began just when it did we cannot positively say, but after the death of the lover in the complicated situation (which we thought proper not to present here) she promptly went into her first and prolonged

sleep. It was a solacing evasion of and oblivion to a difficult situation.

Dr. Spiegel did most of the work on this case, but his material puzzled him. At that point he asked me to help, and I am grateful to him because the case aroused my interest, not so much from the fact that the narcolepsy seemed to represent an evasion but because the therapy produced such striking benefit. In refuting the idea of an organic lesion which resolved spontaneously, I must repeat that these symptoms had continued for nearly twelve years and the patient had been in the hospital for nearly six months, without improvement in her condition, before Dr. Spiegel began to treat her psychologically. One might maintain that whatever lesion was present in the ventricle disappeared at that time, but I question such an explanation. What interested me from the psychotherapeutic angle was the disappearance of a serious and long-standing condition on the basis of psychocatharsis alone.

I have been puzzled for many years as to whether the deep, penetrating and complicated analysis of unconscious mechanisms in psychoanalytic treatment may not at times complicate the patient's problems and settle him in a chronic preoccupation with his conflicts. Dr. Spiegel used a simple method in the treatment of a long-standing and severe illness—the original method of Freud—and the patient promptly began to get well. The thought occurred to me that this case was an outstanding example of the necessity for careful judgment in the choice of the application of psychoanalytic technic; I asked myself whether in certain cases such therapy does not prolong illness by too penetrating and too deep analysis. This is especially important today when the term "brief psychotherapy" is heard so often. What is meant by "brief" is still vague—whether it signifies that the patient is treated only over a short period, that the sessions are short or that the contact with the physician is superficial. Cases of this kind call attention to the need for discrimination in the employment of the method which Freud has made available and to the fact that many patients not only cannot, but should not, be treated by the deepest form of psychoanalysis.

Sequelae and Complications of Convulsive Shock Therapy. Dr. B. L. Pacella and Dr. S. E. Barrera.

The incidence of deaths occurring with the use of metrazol or electric shock therapy has been surprisingly low. Kolb and Vogel estimated a death rate of 1 per thousand among metrazol-treated patients and of 0.5 per thousand in electrical shock-treated material. Cardiovascular disturbances are usually mild, generally occur immediately after the seizure, with the patient exhibiting an irregular, slow pulse, and spontaneously clear up. In our own material hypertension developed in 2 patients subsequent to treatment, but more often lowering of the blood pressure occurred. Evidence of intracranial hemorrhage has not been observed. Pulmonary and respiratory complications are few, although postconvulsive apnea and stridor are commonly observed; these are readily overcome. The effect of treatment on healed or active tuberculosis is not yet clear, but patients with active tuberculous lesions have been treated successfully. Vertebral compression fractures occur in about 20 per cent of patients with whom hyperextension during treatment is employed, but symptoms are mild and disappear in a short time. Fracture of the long bones is extremely rare but may occur in elderly patients. Three patients in our series exhibited dizziness and 2 patients spontaneous convulsions after treatment. Electroencephalograms obtained prior to treatment from the latter 2 patients were abnormal. Histopathologic changes in the brain thus far reported have not been in substantial agreement with each other. Electroencephalographic changes produced by treatment have been largely reversible, although in a few instances they have persisted for periods exceeding six months. Memory defect resulting from treatment is a striking complication but generally disappears in a few weeks. It is concluded that the benefits derived from convulsion therapy in properly selected cases usually far outweigh the possible complications which may occur.

DISCUSSION

Dr. S. Bernard Wortis: Dr. Pacella and Dr. Barrera are to be congratulated on the collection of data indicating that occasionally electric shock therapy can be given safely to the patient with mental disease who has an associated serious medical or surgical illness. Usually the physician will find it advisable to wait for his patient's medical condition to improve. Relative contraindications to shock therapy are severe hypertension, hyperthyroidism, tuberculosis, febrile conditions and active cardiovascular disease; I should be reluctant to advise electric shock treatment for a pregnant woman. The effect of this treatment on the fetus is not known. It is known that small hemorrhages occur as the result of severe convulsive movements, and it may be that such hemorrhages have a harmful effect on the fetus. However, occasionally the severity of the mental illness may warrant drastic treatment.

Since the motor convulsive phenomena are responsible for some of the complications, my associates and I at Bellevue Hospital have given a preconvulsive intravenous injection of sodium amytal. This diminishes the severity of the motor convulsive phenomena and lessens postconvulsive overactivity. For this purpose sodium amytal is safer than curare or betaerythroidine.

Almost every one has come to recognize that the treatment is disappointing for schizophrenia and the neuroses. One can see clinical improvement in patients with paranoid conditions after treatment, but generally the paranoid quality of the personality remains, even though the patient cannot focus on the particular subject that seemed to disturb him before therapy.

Dr. Hubert S. Howe: Certainly, it is through a study of the dangers and complications of this treatment that one will learn how to overcome them. The dangers seem to be remarkably few in view of the violence of the procedure. The question of damage to the brain looms large in the minds of some investigators who have induced convulsive seizures in animals. Others have carried out similar experiments with no cerebral injury. In view of this disagreement, it is necessary for us as psychiatrists to follow the patients who have received this form of therapy and observe the results not only immediately, but months and years, after the treatment. We must ascertain whether their intellectual performance is on a level with their best normal activity. Comparison of electroencephalograms taken before, immediately and six months after completion of the treatment may also be of value. Such a careful followup study is being made at the New York State Psychiatric Institute.

Impairment of memory is the most obvious psychologic complication. This has never been serious or persistent in any of my patients, but from personal communications from other workers and from the literature there is little doubt that persistent incapacitating amnesia has been observed in some persons who have

received a large number of treatments with high voltages. In my experience, a course of from six to eight convulsive seizures is sufficient, and rarely have more than twelve been given during a short period, even in cases of schizophrenia. A few patients who were not completely relieved of depression have returned after a few weeks to have additional treatments. I believe that this is preferable to a longer course in the beginning.

At the Neuropsychatric Institute in Hartford, Conn., the Reiter apparatus is used, and not over 20 to 30 volts of current is employed. Patients treated by this method have no memory disturbance, but the application of the electrodes to the parietal regions and the vertex, instead of the frontotemporal areas, may also be a factor.

I wish to record a protest against administration of these treatments outside a hospital with a staff of trained assistants. Everything possible should be done to protect the patient from fractures, biting the tongue, headache, muscle pains and other minor complications which cause him to dislike and dread the procedure. I have a routine of preinduction medication which seems useful. Just prior to the treatment the patient is given 1 grain (65 mg.) of codeine phosphate and 3 grains (0.195 Gm.) of seconal sodium by mouth. . With this medication we have not had complaints of as severe headache and muscle pains as our patients had frequently experienced before this regimen was instituted. . The memory of after-confusion is less vivid and the whole experience less unpleasant.

I should like to ask Dr. Pacella what he thinks of the results of electric shock with the Reiter apparatus and whether he believes that this form of application will supersede the older method.

Dr. Lothar B. Kalinowsky: I can only agree with the practical conclusions of the authors, for I have worked with them in this field for years. I should like to comment on a few of the most disputed points.

One of the most frequent questions is whether organic changes are produced. My associates and I observed no microscopic changes in the brains of monkeys treated in the same way as our patients (Barrera, S. E.; Lewis, N. D. C.; Pacella, B. L., and Kalinowsky, L.: *Tr. Am. Neurol. A.* **68**:31, 1942). However, there is sufficient evidence that cerebral function is disturbed. Not only are electroencephalographic changes present, but the mental changes give evidence of organic changes. There are the memory defects; with them always go emotional disturbances, and in many patients more dramatic syndromes, even a delirium-like picture, appear. All the known varieties of symptomatic psychoses occurring with infectious-toxic diseases can be seen during a long course of electric shock treatments. But they are reversible, and even the most dramatic mental symptoms of organic origin usually disappear a week after the last treatment, except for slight impairment of memory, which may last longer.

A case which illustrates what Dr. Pacella has mentioned, that the relearning function is not seriously impaired, is that of a physician who was graduated abroad twenty years ago; he was deeply confused during the treatment of a depression and even lost his command of English. A few months later, however, he passed a state board examination.

I have treated several patients with tuberculosis; 2 of them were severely emaciated because they had refused food, and therefore the tuberculosis was aggravated by the mental condition. Both patients did well; one doubled her weight. I have also treated patients with schizophrenia complicated with traumatic epilepsy whose spontaneous convulsions did not increase, but disappeared during and several months after electric shock treatment, probably owing to the usual elevation of the convulsion threshold under convulsive treatment.

As to fatalities, I can only say that in my personal experience of almost 2,000 cases, I have not had a single death. A review of the literature reveals that several of the few fatalities were reported from hospitals where electric convulsive therapy is combined routinely with preconvulsion administration of curare. This indicates the risk of curare, which, therefore, I have not employed routinely, although its use is indispensable in certain cases. I have had no cases of fracture, since I avoid any tight restraint of the patient during the muscular discharge.

Administration of sodium amytal, as mentioned by Dr. Wortis, is recommended for two reasons: to prevent postconvulsive excitement (for this we use it in difficult cases, with excellent results) and to decrease the strength of the convulsion. The latter effect is obtained only with doses of 10 or 12 grains (0.65 or 0.78 Gm.). I have seen this decrease in the strength of the muscular discharge also with other anticonvulsive drugs, particularly with diphenylhydantoin, if these substances are given in amounts near the toxic level.

I wish to stress that, as Dr. Barrera and Dr. Pacella have shown, electric convulsive therapy is not invariably dangerous but has certain complications, and therefore should not be used when not definitely indicated. Its indiscriminate use should be warned against, particularly its constantly growing application in treatment of the neuroses, for many of which the extremely poor results do not justify the risks.

Dr. B. L. Pacella: The Reiter apparatus is an electric shock set, apparently of a new design, which is being used at the Hartford institute, and is still in an experimental phase. However, as Dr. Howe pointed out, it apparently produces substantially less memory defects than the forms in current use, and in some persons no memory disturbance can be detected clinically, even in the patient who had received, according to Dr. Howe, as many as twenty convulsive treatments. Not only does this apparatus employ a lower voltage, but the character of the electrical pulsations, that is the wave form, is somewhat different from that with other machines. The convulsion produced in the patient is essentially the same as that obtained with our present apparatus. The clinical impression of the physicians using it, who have also employed other electric shock sets, is that the therapeutic effects are about the same with all types of machines. There are certain disadvantages which I shall not discuss at present.

The important feature of this new apparatus is the apparently much less pronounced effect on the memory than is noted with use of the other sets. This may be disturbing to investigators who maintain that improvement or recovery depends largely on the disturbance in memory produced by the shock treatment. Another important feature noted in patients treated with the Reiter apparatus is that few electroencephalographic abnormalities are produced, even though a considerable number of convulsions is induced. Dr. Abraham Lieberson, who has carried on electroencephalographic studies on such patients, has shown me tracings obtained from patients who have had a large number of convulsions, in which only slight changes were found, an observation distinctly in contrast to the effect on the brain potentials with use of the present standard electric shock machines, in which the ordinary 60 cycle alternating current is utilized as the shocking stimulus. This observation is difficult to explain.

ILLINOIS PSYCHIATRIC SOCIETY

CLARENCE A. NEYMANN, M.D., *President, in the Chair*
Regular Meeting, March 2, 1944

Cerebral Malaria: An Electroencephalographic Study. DR. MANDEL SHERMAN, Chicago, and MAJOR W. PARK RICHARDSON, Medical Corps, United States Army.

The electroencephalographic investigation was made on soldiers with malaria who were hospitalized primarily for psychiatric observation and diagnosis. These patients presented the following symptoms: nausea and other gastrointestinal disturbances, weakness, headaches and dizziness and varying degrees of depression and lack of interest in their surroundings. Sixty-one patients with these symptoms who had malaria were compared with 30 patients with similar symptoms who did not have malaria. Definite abnormalities were observed in the electroencephalograms of 15 of the 61 malarial patients. This high incidence of abnormalities indicative of cerebral involvement is probably due to the fact that these patients represented selected cases from the malarial population, and not the frequency of cerebral disturbance in the general population.

The electroencephalographic changes included (1) abnormal waves of the delta type, with a frequency of 5 to 9 per second; (2) arrhythmia, which varied in degree from one patient to another, and (3) unusual changes in amplitude, indicating metabolic or other variabilities in the brain.

No change occurred with hyperventilation, such as is noted in patients with epilepsy.

A possible cause of electroencephalographic abnormalities associated with malaria is occlusion of the cerebral capillaries by the malarial bodies. Such an occurrence is not infrequent with malaria and has been pointed out by a number of pathologists. The fact that a high incidence was obtained for these patients although they were selected on the basis of their psychoneurotic symptoms indicates that a large number of cases of cerebral malaria may exist without recognition by the usual clinical methods.

DISCUSSION

DR. M. T. KOENIG, Chicago: How do these changes in the electroencephalogram compare with the records for other infectious diseases, such as typhoid, pneumonia and other conditions accompanied by symptoms of cerebral involvement?

DR. MANDEL SHERMAN, Chicago: The question is a bit too ambitious for present knowledge. From a survey of the literature I know that changes are associated with some of the conditions and that they are not similar to the abnormalities under discussion. With the usual toxic disorders there are no distinct electroencephalographic changes. The difficulty, of course, is to make an electroencephalographic study on a toxic patient. It is not usually done; but when an electroencephalogram is obtained, there are indications of "tension" rather than of the pathologic process seen in the records of the malarial patients.

DR. CHESTER DARROW, Chicago: The authors raised the question of the probable origin of the abnormal waves. The cause suggested, and one which must be considered seriously, is the occlusion of the smaller vessels by the parasites, with focal ischemia giving rise to an abnormal electroencephalogram. However, the authors rightly question the correctness of this interpretation since, if it were the explanation, there should be indications of a focal pathologic process. That such a focus was indicated by the electroencephalographic evidence is obvious from the essential similarity and synchrony of the larger slow waves in the two sets of records. In the record which was presented as more nearly normal there was even greater discrepancy between the two areas. It is questionable whether these effects truly arise from the cortex or represent a generalized cortical disturbance with, possibly, a deeper origin. My associates and I at the Institute for Juvenile Research have been interested in a problem related to the one presented here, namely, the electroencephalographic effects of encephalitis. Mr. Julian Pathman has been making a collection of records in cases of this disease, and there is a striking general similarity between the records he obtains and the records presented here. As the authors suggested, there is also the possibility of generalized damage, possibly arising from anemia or some other pathologic condition affecting the cerebrum as a whole, as well, perhaps, as deeper-lying structures.

I had hoped the authors might present the effects obtained at different stages of the malarial cycle. If one could have electroencephalographic records during the phase of actual fever, as well as before and after it, one might have a clue to the effects on cerebral activity of the actual disease process in the brain, as contrasted with possible residual effects.

Notwithstanding that abnormal results are obtained in a limited percentage of cases, it appears that a new field may be opened for the application of electroencephalography.

Homosexuality, Transvestitism and Psychosis: Study of a Patient Treated with Electric Shock. DR. SAMUEL LIEBMAN, Chicago.

The relation of homosexuality and transvestitism to psychosis has interested many psychiatrists. I had the good fortune to study a patient at the Norwich State Hospital (Conn.) who presented all these conditions.

The patient had been adopted at about 1 year of age by a maladjusted family. In this peculiar environment he early showed feminine interests. As he grew older, his interests became less masculine, until he became overtly homosexual, transvestitic and psychotic. The anamnesis revealed that 2 male siblings were homosexual and that the maternal side of the family had been heavily tainted for at least two generations.

After the administration of electric shock therapy the patient recovered from his psychosis and gave up his transvestitism. He was kept under observation for almost a year. Psychologic studies were made at intervals throughout the period of hospitalization and the subsequent period of observation. The changes in the patient's symptoms, ideation and mood under the conditions of hospitalization and follow-up study were interesting.

DISCUSSION

DR. D. B. ROTMAN, Chicago: The patients with transvestitism I have seen have been without psychosis; it seems to me that the conflicts in the present case of transvestitism precipitated the mental condition and that the cure effected by electric shock therapy was of schizophrenia, not of transvestitism. The more interesting cases of transvestitism I have seen have concerned persons who were not effeminate at all. I have particularly in mind a patient whom I had under treatment for six months. He was referred to me because

his expense account had gone so high that his father could not keep him in college any longer. He was using all his school money to buy feminine apparel from a fashionable dressmaker. This he wore secretly in his room before the mirror. But he had none of the attributes of effeminacy described in Dr. Liebman's case. At one time in his career he was so intent on appearing as a female that he insisted on undergoing an operation which would make him really look like a female when he put on the clothes he wished to wear in secret. He was able to finish a college course, that is, a period of four or five years, without detection of this impulse by his intimates.

Another point of interest to me in Dr. Liebman's paper is the fact that this person was a female impersonator. In court my colleagues and I see persons of this type in large numbers. Transvestitism is especially common among so-called male prostitutes. But I have never seen such a person thrown into a psychotic state by conflicts over his condition. Given a patient of intelligence, who is a transvestite and is not psychotic, is one, with present knowledge, justified in applying shock therapy? Has any one the courage to apply this form of treatment to such a condition? I feel that one of the finest research problems which could be undertaken in this community would be the hospitalization of a group of so-called sexual psychopaths with no abnormalities of the endocrine glands for a trial of shock therapy. I do not regard the shock treatment in the author's case, which was for schizophrenia, as at all related to such a problem.

Dr. M. T. Koenig, Chicago: Dr. Rotman's comments are interesting. The case struck me somewhat differently. If one will disregard the transvestitism for the present and consider this patient as he arrived at the hospital, overdressed, overdecorated and at the same time wearing men's clothes, and will follow the course of his psychosis and note his grandiose ideas, one will have the impression of a manic-depressive psychosis, of which the transvestitism was only a manifestation. The further progress of the condition seems to confirm this diagnosis. The irritability and paranoid trends are often observed in patients with manic states toward the time of recovery. Then with electric shock treatment the manic patient duly passes through his depressed state.

Dr. Victor E. Gonda, Chicago: I know of a case exactly like the one Dr. Liebman presented. A well to do family adopted a child from the Evanston Cradle. At the age of 15 he was observed dressed in girl's attire and masturbating openly. The two policemen who found him took him home to his foster parents. Since the condition was serious, at least on the borderline of a psychosis, my colleagues and I undertook to treat the boy with electric shock, I am sorry to say, without result. It may be that we did not give him enough treatments.

As far as I know, transvestitism has not been treated successfully anywhere; it would be nice to start something new in Chicago.

Dr. Samuel Liebman, Chicago: I avoided making a diagnosis, for I did not want to commit myself. The only reference in the available literature in relation to the shock therapy of this personality disorder was that of Owensby, who treated 6 homosexual patients with metrazol. He claimed good results but did not follow his patients for any length of time. They were primarily transients, and I doubt the validity of the results.

The case I reported was worked up to prove to the other members of the staff at the Norwich State Hospital that environmental and psychologic factors are important in the development of personality disorders. The investigation brought out the profuse records of the other members of the family, but that is not a problem to be dscussed now.

The Conditioned Aversion Treatment of Chronic Alcoholism: Preliminary Report. Dr. J. V. Edlin, Dr. R. H. Johnson, Dr. Paul Hletko and Dr. Gert Heilbrunn, Chicago.

Owing to its known gravity and prevalence, the syndrome of chronic alcoholism does not invite an aphoristic restatement. Methods of treatment have in general pursued two goals: (1) the management of the withdrawal period and the immediate restoration of the patient's well-being, and (2) the inculcation of permanent sobriety, by utilization of individual or group psychotherapy, occupational and recreational activities and pharmacologic mediums. The achievement of the first goal is usually attained—the actual problem, however, arises after the acute withdrawal symptoms have subsided.

Reliable means of therapy were continually sought, and the new approach through establishment of an aversion to alcoholic beverages was deemed worthy of a thorough trial. The treatment consists essentially in establishing a reflex aversion to the sight, smell and taste of alcoholic beverages by means of an emetic. Eighty-five patients, with an average age of 38 and an average period of addiction to alcohol of twelve and one-half years, were treated. Of this total of 85 patients, 7 were treated outside the hospital as private patients. Four patients, or 58 per cent of this private group of 7 persons, have abstained from alcohol from three to seven months; 2 patients have relapsed, and reliable information on the fourth patient is unavailable.

A statistical evaluation of the results obtained with the entire hospital group cannot reflect the true merit of the treatment, and it is more advantageous to consider only the hospital patients who completed treatment at least five months ago. Sixty-four patients were treated between April and September 1943. Fifteen patients, or 23 per cent, are known to have remained abstinent for five to ten months. Follow-up information is unavailable on 22 patients, and 27 patients are known to have relapsed. This figure of 23 per cent is in contrast to the 58 per cent of favorable results obtained with the small group of patients privately treated.

The principal source of discrepancy in the results presented itself in the patient's sociologic situation as the probable reflection of his emotional and psychologic status. A survey of the records of the hospital patients disclosed a rather inferior social and financial situation, whereas all patients of the privately treated group and 11 of the 15 patients who were successfully treated at the hospital had a superior sociologic rating.

We concur in the consensus that every alcoholic patient suffers basically from a personality disorder and that the alcoholic debauch represents an escape from conflict. It is realized that the aversion treatment does not represent a "cure" at all—it must be regarded merely as a method to render the addictee abstinent for a certain period, during which psychotherapy, whether of the group form, such as attendance at meetings of the Alcoholics Anonymous, or individual, can be instituted and gain ground.

DISCUSSION

DR. JULES MASSERMAN, Chicago: This work by Dr. Edlin and his associates is to be highly commended on a number of counts: a well defined problem, a consistent technic, adequate follow-up studies and, best of all, an analytic and critical evaluation of results in the light of relevant and important psychologic and social factors. Moreover, the authors reach conclusions that are quite in accord with the modern psychodynamic concepts of alcoholism and its therapy—and it is perhaps only in this connection that I was assigned to supplement their discussion.

First, the authors correctly use the theoretic term "conditioning," not in the jejune pavlovian sense of mechanical reflexology, but, rather, to represent a process of adaptation in which meaning and motivation play essential dynamic roles. Meaning is never independent of the subject's conscious or unconscious interpretations of the situation; for this reason, a patient detained in a hospital and made to vomit an ipecac cocktail in a doctor's laboratory will obviously resolve never again to drink—that is, never again to drink an ipecac cocktail in a doctor's laboratory. But this resolution will not necessarily prevent him from imbibing good Scotch with a sympathetic friend at the nearest bar when he is sufficiently in need of the effects of alcohol and is free to obtain it on his own terms. As to motivation, Dr. Edlin and his coauthors showed that patients who after therapy again experience the need to escape from pressing economic and social problems are apt to resume their alcoholic intake under the stress of anxiety-ridden living. The final question as to the adaptative choice of the drug then arises: Why does a neurotic person take to alcohol? By what pharmacologic magic does alcohol fill the needs of a neurotic person so specifically that he will seek it avidly to the point of intractable addiction? Rado, Knight, Schilder and others pointed out the oral, homosexual and other symbolic unconscious satisfactions that alcoholism facilitates, but their valuable psychoanalytic studies still did not explain the special needs for the drug itself rather than for other forms of oral indulgence, or the corresponding addiction of patients with similar neurotic mechanisms to sedatives, hypnotics and opiates not necessarily taken by mouth or in homosexual camaraderie. However, recent experimental studies in my laboratory may furnish a remote clue to this problem. Briefly, it was observed that when alcohol was administered to normal animals, they were no longer sensitive to the complex demands of their environment and reverted to more simple, directly satisfying, though somewhat disorganized, activities. When an experimental neurosis was induced in these animals by subjecting them to a severe motivational conflict, alcohol was again successful in abolishing complex "neurotic" adaptations, such as inhibitions, phobias and compulsions, and in this way the drug appeared to give the animal demonstrable relief. Moreover, some of the animals soon associated the drug with these effects and began to prefer foods that contained alcohol to foods that did not. In other words, the animals became alcohol "addicts" and remained so until the neurosis was relieved by some form of therapy and the need for the effects of alcohol thus abolished. If the qualifications necessary in evaluating such animal experiments are neglected for the moment, one fact emerges: A neurosis is a psychobiologic tension state that is symptomatically relieved by alcohol. When this is translated, however broadly, into operational terms, one may confirm experimentally the clinical observation of Edlin and his co-workers, and nearly all others in the field, namely, that an alcoholic addict will continue to seek and imbibe his drug as long as his neurotic needs for its pharmacologic and psychologic effects continue. The treatment of alcoholism, then, must be more than merely symptomatic: In the last analysis, the underlying neurosis must be attacked by every medical, psychologic, economic and social means at one's command. Obviously, the authors of the paper have reached the same implicit conclusions.

DR. CHESTER DARROW, Chicago: Were the patients informed that there was ipecac in the drink?

DR. FRANZ ALEXANDER, Chicago: The two papers presented here in which the shock therapy for psychosis and the treatment of alcoholism were considered have one feature in common—they represent something which might be called symptomatic therapy, an approach which the rest of medicine tries to replace more and more with the etiologic attack. This is not meant as a criticism; it is merely a statement of fact. Dr. Masserman's films forcefully demonstrated that alcoholism is a symptom, not a disease. Only neurotic cats prefer alcohol, for it relieves them of certain conflicts. The conflict is the cause and alcoholism the resulting symptom.

I must, however, defend Dr. Rado from Dr. Masserman's criticism, because in his paper on drug addiction he came to similar conclusions, namely, that alcohol, through its narcotic effect, relieves basic conflicts and thus creates the craving for alcohol. This is also true of morphine and opium. The main issue is that alcohol, by its narcotic effect on the higher centers, temporarily removes inhibitions and thus relieves the complex conflicts of emotional life. Probably something similar takes place in shock treatment, except that its influence on the higher centers lasts somewhat longer. I wish to emphasize that both conditions discussed tonight, alcoholism and schizophrenia, are chronic disturbances of long duration. In my experience of twenty-two years, I have learned to look on both the psychotic and the alcoholic patient from a long range point of view. I cannot see the validity of speaking of a cure of such a condition when the result lasts only about nine months. What is nine months in the life of an alcoholic addict? I should speak of the symptom-free periods as remissions. Remissions of six to nine months are common with alcoholic patients, who from time to time "go on the wagon."

The psychotic patient whose case was described here was treated with shock; he had a relapse and was given shock therapy again; the chief result was the change in form of his symptoms. For a while he was even free from symptoms. However, in the case of the patient with a psychosis, combined with transvestitism, a remission of nine months or a year does not mean much. The underlying condition is still there; otherwise why should he relapse again and again? And if such a patient does not relapse, I should require a thorough investigation of the situation in order to decide whether the remission is not due to changed conditions. In this type of therapeutic research I should like to see it taken for granted that alcoholsm or the manifestations of schizophrenia are symptoms, and not the basic condition. In internal medicine one is not much impressed when the patient's headache is relieved by administration of acetylsalicylic acid and the basic condition is left unchanged. Psychiatrists are not yet clearly aware of the difference between the symptomatic approach and the etiologic attack on the basic condition, and they continue to forget that the symptoms are nothing but the self-curative attempts of the organism.

Dr. Edlin and his associates were aware of the symptomatic nature of their treatment, but I should have liked even more emphasis on this part. Dr. Liebman's patient exhibited schizophrenia, transvestitism, homosexualism and, finally, criminal behavior. I wonder what he will show after a new series of shock treatments?

Dr. Conrad S. Sommer, Chicago: I discussed this subject with the authors before they began their study and had an agreement with them that certain criteria should be followed in the selection of cases. However, I presume that in order to get enough cases to serve as a basis for the completion of the paper some of these criteria were disregarded. Since, however, the criteria apply to the selection of cases with regard to the social and vocational adjustment, I should like to indicate them briefly: 1. The patient should be in sound physical condition, and the alcoholism should not be accompanied by psychosis. 2. The patient should show interest in therapy and voluntarily apply for it. 3. There should be evidence of family support and interest in the treatment, as demonstrated by a relative or a close friend. 4. The patient or the family should supply the necessary alcoholic beverages as further evidence of his or their interest and as an indication of cooperation in follow-up studies. 5. The conditioned reflex treatment is successful only as already mentioned, in producing a temporary aversion to drinking. The conditioned reflex treatment will not make a new man out of one who has never made a successful adjustment in the first place. But it conceivably can, and, it is to be hoped, will give an alcoholic person enough of a breathing spell from his alcoholism so that his will to stop drinking has a chance to assert itself. Hence, a futher requirement for admission to the conditioned reflex treatment is that the patient shall have had at least three years of successful work experience.

I suggest that the authors reevaluate their successes and failures in the light of their observance of these criteria.

Dr. Gert Heilbrunn, Chicago: The discussions need no further comment; it is sufficient to stress again that the conditioned aversion treatment cannot be considered a cure for alcoholism. However, in a considerable number of cases it establishes a period of abstinence which may and should be utilized for a psychotherapeutic approach. My colleagues and I agree with Dr. Alexander in his observation that alcoholic patients may have spontaneous periods of abstinence lasting from six to nine months. The overwhelming majority of our patients, however, had indulged in the use of alcohol continuously, so that there was no opportunity for a psychotherapeutic approach to gain ground.

In response to Dr. Darrow's question, the patient is informed before the start of the therapy that he will receive a medicament mixed in his first drink to educe the obnoxious qualities of the alcohol.

CHICAGO NEUROLOGICAL SOCIETY

R. P. Mackay, M.D., *President, in the Chair*
Regular Meeting, March 14, 1944

Herniation of Cervical Intervertebral Disks. Dr. Paul C. Bucy and Dr. Harvey Chenault.

Two cases of herniated cervical intervertebral disk were reported, with compression of the seventh cervical nerve root in 1 and of the sixth cervical nerve root in the other.

In the first case, that of a man aged 41, herniation of the intervertebral disk between the sixth and the seventh cervical vertebra, with compression of the right seventh cervical root, occurred as the result of a fall on an icy street. This condition gave rise to repeated attacks of severe pain just below the medial part of the spine of the right scapula and to persistent paresthesias of the thumb and the index and middle fingers and the radial border of the forearm, all on the right side. Removal of a small piece of herniated cartilaginous material through a partial hemilaminectomy opening gave immediate and complete relief from all symptoms.

In the second case, that of a women aged 31, an automobile accident caused herniation of the intervertebral disk between the fifth and the sixth cervical vertebra, causing compression of the left sixth cervical nerve root. She experienced immediate pain at the base of the neck on the left side. A few days later this pain began to radiate across the shoulder, down the outer aspect of the arm and out to the end of the thumb. It was usually a constant dull ache, but moving the arm or the neck often evoked a sudden, sharp burst of pain which radiated from the neck down the arm and into the thumb.

Roentgenographic examination disclosed loss of the normal curvature of the cervical portion of the spine, reduction in the intervertebral space between the fifth and the sixth cervical vertebra and slight hypertrophic bony changes at this joint.

These 2 cases emphasize that the sensory area supplied by the sixth cervical root centers about the thumb, while the sensory distribution of the seventh cervical root is concerned primarily with the index finger.

DISCUSSION

Dr. Frederick Hiller: On what clinical evidence do the authors make the differential diagnosis of herniated disk and secondary narrowing of the neural foramens?

Dr. Adrien Verbrugghen: I have reported 4 cases of this condition before this society (Prolapsed Cervical Intervertebral Disks, Arch. Neurol. & Psychiat. **52**:251 [Sept.] 1944) in which the typical signs were not presented. In 2 cases the index finger was the only one involved, but in 2 other cases, in which the sixth and seventh roots were compressed, there was no anesthesia or any other neurologic sign except in the roentgenogram. As a matter of fact, this afternoon my associates and I operated in another case in which there was a narrow disk between the fifth and the sixth cervical vertebra, with no objective neurologic signs, but with great pain. I should like to ask Dr. Bucy whether he has any explanation for the fact that the postaxial elements of the root are more involved than the preaxial elements in the sciatic and in the cervical syndrome. I have asked many people, but so far I have not had a good answer. I have no answer myself.

Dr. Paul C. Bucy: I can conceive of there sometimes being great difficulty in differentiation from arthritis with compression of the root either by thickening of the soft tissue or by bony proliferation at the intervertebral foramen. In most cases the differentiation will rest on several factors. One is the localized nature of the pain. Usually a patient with a herniated disk is insistent on the localization of his discomfort, whereas the patient with arthritis of the spine has more diffuse discomfort, which is often bilateral and involves more than one root. With arthritis the discomfort is often

more gradual in its development than that with herniated disk. The roentgenogram is helpful in some cases, although it is conceivable that a patient may have both arthritis and a herniated disk.

It is possible to have a herniated vertebral disk and a normal roentgenogram, as occurred in the first of the 2 cases reported. The roentgenographic signs when present are not striking. They are limited to one intervertebral space. That space is reduced in width as compared with all the other spaces; the normal curvature of the cervical part of the spine is lost at the point of the herniation, and there may be proliferative bony changes, which are limited to that level.

Paralysis of Nerve Induced by Direct Pressure and by Tourniquet. DR. DEREK DENNY-BROWN and DR. CHARLES BRENNER.

This paper was published in the January 1944 issue of the ARCHIVES, page 1.

DISCUSSION

DR. PAUL WEISS: I am somewhat embarrassed to be called on for comment, for I should prefer not to have to contradict the distinguished visitor.

I have been working on experimental nerve compression for two years and, with my collaborators, have studied well over 100 cases. We have observed and described the following effects: (1) pressure block of conduction; (2) preservation of axis-cylinders in the compressed zone; (3) edema proximal to the constriction; (4) damming of the axoplasm proximal to the constriction, and (5) swelling of degenerated fibers distal to the constriction.

Dr. Denny-Brown's pictures furnish beautiful confirmations of our observations. They also add a new point in understanding of the fate of myelin under compression. I must disagree, however, with the interpretation given by Dr. Denny-Brown that these phenomena are due to interference with the blood supply rather than to a direct disturbance of the nerve fibers. My colleagues and I have presented seemingly conclusive experimental evidence that constriction affects the nerve fibers directly. Some of the evidence may be briefly restated.

Pressure Block.—In joint experiments with Dr. Hallowell Davis, excised peripheral rat nerves were provided with fitting cuffs of living artery and stimulated at one end, and oscillographic records were taken from the other end. When the arterial cuffs were made to contract by application of epinephrine, conduction of impulses was blocked within a few minutes. On redistention of the vascular cuffs conduction returned. That the block was due to the mechanical disturbance, and not to ischemia and anoxia, is plain not only from the fact that blood supply to the nerve was absent and access of oxygen to the surface of the nerve was as much restricted in the unconstricted as in the constricted cuffs, but from the promptness with which the block developed.

Dr. Denny-Brown has referred to Grundfest's observation that nerve conduction is abolished only by very high pressures. In this he overlooks the fact that in Grundfest's experiments the whole nerve was enclosed in a medium which was placed under even pressure, so that the fibers could remain intact, whereas local constrictions always produce displacement of neuroplasm. Obviously, conduction is blocked by this local disorganization of the axon, rather than by pressure as such. Grundfest's results are therefore of no relevance to the problem of nerve constriction. Moreover, Dr. Denny-Brown has emphasized that tourniquet block often affects the motor fibers alone, to the exclusion of the sensory fibers. Can sensory fibers subsist in anoxia? If not, anoxemia cannot have been severe enough to account for the motor block.

Preservation of Compressed Axis-Cylinders.—The fact that axons in a constricted zone fail to undergo wallerian degeneration, as observed by Ramón y Cajal, Stroebe and us, is beautifully illustrated by Dr. Denny-Brown's slides. But, again, this effect cannot be laid to ischemia because it can likewise be obtained in vitro. My colleagues and I have shown that in excised nerves placed in isotonic solution of three chlorides U. S. P. and subjected to partial constriction wallerian degeneration is inhibited throughout the constricted portion, whereas the mere covering of the surface without constriction had no effect. Therefore, constriction interferes with fiber degeneration directly, and not by way of ischemia.

Edema.—Dr. Denny-Brown describes swelling of the nerve on both sides of a constriction. My associates and I have previously described the same phenomenon. However, we have insisted that the nature and origin of the swellings are altogether different on the central and on the peripheral side: Centrally there is accumulation of interstitial liquid between the nerve fibers, while distally the individual fibers become vacuolated and swell but remain closely packed. In line with common terminology, we designate only the former swelling as edema. Dr. Denny-Brown prefers to call both conditions edema. I am glad to note that the difference of opinion between him and me in this matter has arisen merely from his use of the same term for two different phenomena. The interstitial edema is proximal. This position indicates that it is not primarily of vascular origin. My associates and I have concluded that it results from the damming up of endoneurial fluid in centrifugal motion. We have recently confirmed the existence of this endoneurial flow by radioactive tracers. At any rate, the proximal interstitial edema must not be confounded with the traumatic swelling of the distal fibers.

The preceding critical comments bear on matters of evidence and interpretation. They should not be allowed to overshadow my admiration for the excellence of Dr. Denny-Brown's observations and illustrations. Furthermore, if I advocate the view that constriction acts on nerve and nerve fibers directly, I am referring to the primary effects only. There is no doubt that ischemia will likewise leave its mark on the nerve through secondary effects. However, to distinguish the direct from the indirect effects must remain a matter of future analysis, rather than one of mere assertion.

DR. FREDERICK HILLER: I have been fascinated by this paper, as would be any one who has studied the problem which Dr. Denny-Brown has discussed. My associates and I have carried out experiments concerned, among other problems, with the effect of nerve traumatization as encountered particularly in gunshot wounds. The results of these studies are soon to be published. I can confirm Dr. Denny-Brown's observations. Nerve contusions produced by a bullet that has passed through the thigh of a cat, more or less close to the sciatic nerve, afford a particularly good opportunity to study the effect of trauma on the nerve. We observed that the traumatization varied in degree in the different fasciculi. Cats were allowed to survive the trauma from several days to many weeks, and we observed the nature of the traumatic effect in its degenerative and regenerative phases. The traumatized nerve shows not only the well known wallerian degeneration but areas of

necrosis, the latter differing histologically from the former. It is surprising that these necrobiotic phenomena should have escaped the notice of practically every one who has worked on the problem of nerve damage and nerve regeneration. They can be seen not only in traumatized portions of a nerve but in grafts in which lack of circulation leads to a breakdown of the ectodermal elements. The necrobiotic destruction of the myelin fails to show the characteristic phases of the wallerian degeneration, namely, the typical dark-stained myelin globules and the large fat droplets. The necrotic decomposition products fill not only the endoneural tubes but, as Dr. Weiss mentioned, the intertubular spaces as well. Edema is seen frequently. I agree with Dr. Denny-Brown that an ischemic lesion is the probable explanation of this sort of tissue reaction. The necrobiotic process apparently has a stimulative effect on the endoneural cells. A strong mesodermal proliferation takes place in traumatized nerve fasciculi, leading to more or less profound obliteration of the original structure of the endoneural tube. Proliferation of Schwann cells and regeneration of nerve fibers follow the proliferation of the mesodermal endoneurium, and the arrangement of the regenerated nerve fibers becomes just as irregular and confusing as that of the mesodermal cells and fibers. The isomorphous structure of a normal nerve, retained in the neurotization of a nerve in secondary degeneration, becomes heteromorphous in traumatized portions of a nerve, as well as in most nerve grafts. Traumatized myelin may also form a lasting barrier to the outgrowth of axons, leading to the formation of Perroncito spirals. The general belief that these spirals are the effect of connective scar tissue, with obstruction of nerve regeneration, is certainly wrong.

DR. DEREK DENNY-BROWN: I am grateful to the discussers for bringing out so many interesting points. Dr. Weiss differs from me in some respects, partly with regard to the length of nerve compressed and partly with regard to his in vitro technic. The preservation of myelin tubes with loss of nuclear staining in the zone of severe compression, and with degeneration on either side of that zone, seems to me to warrant use of the term "preservation necrosis." It is not clear to me that nerve compressed between cover slips in vitro should be as well oxygenated at its center as at its periphery, and I suspect therefore that factors other than pressure, delay wallerian degeneration, but I am not familiar with the technic.

The difference between Dr. Weiss's view of edema and mine is derived mainly from a difference in opinion as to the nature of the swelling of a nerve distal to a compressed zone. The nerve fibers are more swollen distally; I agree that there may be less endoneural fluid in proportion, but would point out that the nerve fibers are then in degeneration and are themselves edematous. I prefer therefore to regard both the proximal and the distal swellings as edema.

I am not wholly satisfied that vascular stasis is the whole explanation of edema, for if it were the histiocytic infiltration and the endoneural proliferation would still have to be accounted for. I was greatly interested in Dr. Hiller's description of the early loss of myelin and of preservation of Schwann sheaths in nerves contused by a bullet. I have a suspicion, derived from experiments on percussion of nerves, that fragmentation of myelin is the primary cause of the histiocyte response. The endoneural reaction remains for months after the cause of compression is removed and may be the only residual sign of a compression lesion. The mechanism of the endoneural response is tied up with the whole problem of the cause of neuroma.

Injuries of the Vertex of the Skull with Special Reference to the Paracentral Lobules of the Brain. DR. JOHN R. GREEN and DR. ERIC OLDBERG.

Two cases of bilateral injury to the paracentral lobules of the human brain are presented. The influence of such lesions on sphincter control is reviewed and discussed. The superficial clinical similarity between symptoms and signs of injuries to the spinal cord and corresponding indications of lesions of the paracentral lobules is pointed out, and suggestions with regard to the differential diagnosis are made.

This paper was published in full in a previous issue of *Surgery, Gynecology and Obstetrics* (**79**:267 [Sept.] 1944).

DISCUSSION

DR. DEREK DENNY-BROWN: Bilateral lesions of the paracentral lobules must be rare. I remember 2 cases of such lesions, in each of which loss of pain and touch was present in the lower extremities, as described by Foerster, a symptom making their resemblance to cases of lesions of the cord even more complete. I have no explanation for this phenomenon.

Micturition is a roundabout and indirect voluntary act, comparable to salivation. It would seem that the inhibition of an inhibition would best explain the course of events. There is no convincing evidence that the process can be initiated from any region of the motor cortex. Yet there is no doubt that lesions of the parietal area can interfere with the function, making voluntary micturition difficult or impossible. Bilateral lesions of the frontal area, on the other hand, facilitate the process and lead to incontinence. In the cases I recall, the bilateral lesions of the parietal area had also caused loss of position sense and hypotonia in the lower limbs, and the dysuria then appeared to be correlated with the underactivity of reflexes shown by the hypotonia. In the cases presented by Dr. Green and Dr. Oldberg the condition was described as spastic, and this observation appears to set the depression of micturition aside from the general state of other reflexes. Perhaps the difference would have been less pronounced with longer survival.

Book Reviews

The Management of Neurosyphilis. By Bernhard Dattner, M.D., J.D., with the collaboration of Evan W. Thomas, M.D., and Gertrude Wexler, M.D. Foreword by Joseph Earle Moore, M.D. Price, $5.50. Pp. xiii, plus 398 and 27 tables. New York: Grune & Stratton, Inc., 1944.

Dattner's book comes at the beginning of a new era, the penicillin era, in the treatment of neurosyphilis. While this particular drug is still in its infancy, Dattner can look back on two decades or more during which the treatment of neurosyphilis has been revolutionized by the introduction of malaria and pentavalent arsenicals. He consequently gives a scholarly presentation of what has been accomplished between the two world wars in a battle against the disease with which he has been closely identified.

The author brings a freshness of view to the subject. Instead of dealing with the clinical symptomatology and differential diagnosis of neurosyphilis, he relies for both diagnosis and prognosis, and even for therapeutic control, on examination of the spinal fluid. Instead of describing the time-honored intravenous and intrathecal treatments, he jumps right into a discussion of malaria therapy, insisting that as soon as the diagnosis is made the patient should be inoculated. At the same time, however, he gives the historical background and development of various other methods of therapy, with fairly detailed discussion of the favorable and unfavorable results. The discussion is so detailed at times that the author is apt to submerge his own outstanding observations in the large amount of material collected from the literature.

This work is rather strictly a clinical survey, written for the physician who will treat neurosyphilis. Its emphasis on the minutiae of spinal puncture will strike the average physician as absurd in view of the fact that he has been doing spinal punctures since he was a medical student. The same may be said for the laboratory tests, for which the therapeutist relies on the clinical laboratory. A detailed consideration of these procedures does not have a place in a work of this type. More helpful would be a discussion of the relative values of the complement fixation and the flocculation tests and the variations in the colloidal reactions. A chapter on the pathology of the disorder and its response to therapy would also be welcome. Theoretic considerations are given their proper emphasis, and social aspects are handled in a paragraph that deserves to be quoted because of its idealism.

"Only a few words are necessary to refute the objections frequently raised that the modern therapeutic methods in general paresis [dementia paralytica] quite often prolong the life of a patient without enabling him to return to his former occupation and to resume his social functions. These patients put a burden on the community because they must be cared for in state institutions. It has been suggested that a preliminary selection of patients ought to be made, to exclude from the benefit of treatment those patients who offer little chance of social recovery. From a strictly medical point of view this suggestion does not even deserve discussion. How are we going to decide whose life should be saved and whose sacrificed? Who can determine in every case what the end results of therapy will be? It is the duty of the medical profession not to waste time with fruitless attempts at treating late neurosyphilitic patients by methods that time and again have proved ineffective, and not to wait until clinical symptoms manifest themselves even to the layman. We cannot be held responsible when the pathologic process can only be arrested on a low level, because the patient was delivered into our care too late. Furthermore, if new therapeutic methods are to be tried, they should be applied exclusively to those patients in whom procedures that are generally accepted as effective have failed, or to patients who are so far advanced that no therapy offers good prospects of recovery."

Dattner's collaborators deserve much credit for maintaining readability in this important work. The reviewer recalls some fatiguing hours spent in wrestling with the idiom of Dattner's previous (1933) work on the subject. The bibliography and index render the book a first rate secondary source for the researcher of the future who will be concerned with the malaria era of neurosyphilis.

News and Comment

AMERICAN NEUROSURGEONS INVITED TO THE FIRST SOUTH AMERICAN CONGRESS OF NEUROSURGEONS

The First South American Congress of Neurosurgery will be held at Montevideo, Uruguay, March 1 to 4, 1945. An invitation to attend the Congress has been officially extended to North American neurosurgeons by the president, Prof. Dr. Alejandro H. Schroeder. Prof. Agdo. Dr. Román Arana Iñignes, Montevideo, Convencion 1287, is General Secretary of the Congress.

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASES

The Association for Research in Nervous and Mental Diseases, at its annual meeting held in New York on Dec. 16, 1944, voted to center its program for the meeting a year hence on the subject of epilepsy and convulsive disorders. Officers for the coming year are: president, Dr. William G. Lennox; vice presidents, Dr. H. Houston Merritt and Dr. Wilder Penfield, and secretary-treasurer, Dr. Thomas E. Bamford Jr.